CLINICAL SESSION • DENVER • DECEMBER 2 - 5, 1952

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THE JOURNAL

OF THE

American Medical Association

Volume 149, No. 14 — Published Weekly at 535 North Dearborn Street, Chicago 10, Illinois. Subscription, $15. Single Copy, 45 Cents — August 2, 1952

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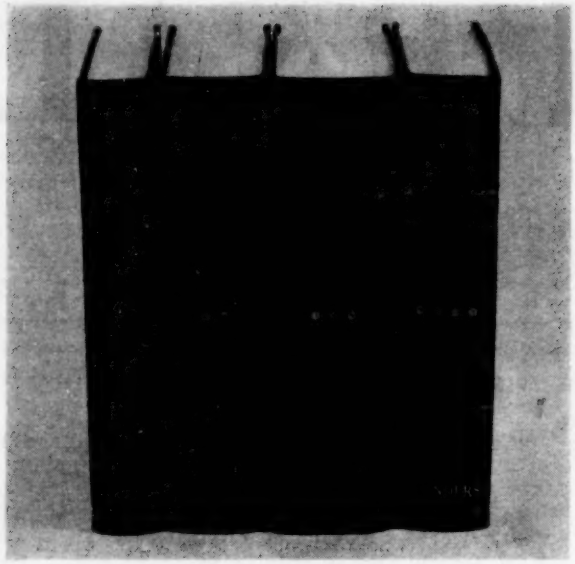

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THE JOURNAL
of the American Medical Association
Published Under the Auspices of the Board of Trustees

VOL. 149, NO. 14 CHICAGO, ILLINOIS AUGUST 2, 1952
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RECENT ADVANCES IN THE MEDICAL TREATMENT OF CIRRHOSIS OF THE LIVER

Sidney A. Portis, M.D.
and
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The incidence of cirrhosis of the liver is increasing. Whereas previously it was seen mostly with alcoholism or malnutrition or as a complication of cholecystitis and cholelithiasis, physicians today are confronted with additional causative factors. The widespread epidemic hepatitis of World War II produced a sporadic inoculation of persons hitherto never exposed to the virus of infectious hepatitis. The etiological relationship of acute infectious hepatitis to cirrhosis of the liver is favored by most authors.[1]

Sulfonamides and other hepatotoxic agents have taken their toll of the liver. Aureomycin has been rather extensively used in the treatment of acute and chronic hepatitis. Recently Lepper [2] reported that, among 14 patients given large doses of aureomycin for serious infections, both by mouth and intravenously, 7 showed clinical evidence of liver dysfunction. Furthermore, necropsy in five and biopsy in one of these cases showed pathological changes in the liver cells; however, the doses of aureomycin used are now considered to be excessive.

Finally, the establishment of blood banks and the use of nonirradiated plasma have resulted in serum homologous hepatitis in some patients and have made cirrhosis of the liver a disease of serious import. No longer can one regard blood transfusions as an innocuous procedure unless the medical history of the donor is known.

GENERAL MEASURES

Certain general measures are applicable in the treatment of all types of liver disease. The recognition of the cause of the liver disease is necessary for effective therapy, and removal of the causative factors assumes a major role whenever they can be determined. In the treatment of jaundice one is constantly confronted by the immediate question of whether one is dealing with a medical or a surgical problem. It may not be amiss at this time to emphasize the importance of cholecystectomy and common duct exploration when indicated as a therapeutic measure in the treatment of liver disease. It is well established that cholecystitis usually produces hepatitis, the degree depending on the resistance of the liver on the one hand and the severity of the inflammatory process in the biliary tract on the other. We are firmly convinced that cholecystectomy should be done whenever cholelithiasis is found, in order to prevent liver damage. Certainly the morbidity and mortality of operative intervention can be markedly decreased if such operations are done before liver damage supervenes or when the liver damage has been improved by the therapeutic measures outlined above. This matter should be seriously considered unless there is a definite contraindication for operative intervention. In our experience contraindications become fewer when a careful evaluation of a surgical risk is made and scientific management is substituted for the haphazard surgical procedures previously employed.

It is preferable that the treatment be carried out in a hospital, where repeated studies of the progress of the disease may be made. When the liver damage is more than minor, it is best also to keep the patient in bed. The use of drugs should be avoided as much as possible, and it should be kept in mind that even the commonly used barbiturates and sulfonamides can impair the function of the normal liver and constitute an added strain on a damaged liver.

Constipation also is an added strain and should be treated with mild laxatives. Bile acids are preferable to bile salts because they produce choleresis and therefore decrease the viscosity of bile. Dehydrocholic acid may be used, 3 to 5 grains (0.20 to 0.30 gm.) three times a day. It not only is a laxative but helps to reduce intrahepatic bile capillary pressure. Furthermore, if the constipation is interdependent on overplay of the sympathetic nervous system and inactivity of the parasympathetic nervous system, parasympathomimetic drugs, like neostigmine (prostigmin®) and benzpyrinium (stigmonene®) bromide, stimulate the gastrointestinal tract, so that perfectly

Read at the Clinical Session of the American Medical Association, Los Angeles, Dec. 4-7, 1951.
Dr. Portis is from the Medical Departments of Michael Reese Hospital and the College of Medicine of the University of Illinois.
The bibliographic references have been omitted from THE JOURNAL because of lack of space; however, they are included in the authors' reprints.

normal bowel movements are possible without irritation of the lining of the bowel. If one prefers other preparations, however, saline laxatives, effervescent sodium phosphate, or magnesium citrate are much better for the patient than the harsher magnesium sulfate or similar drugs, which, we feel, irritate the intestinal tract too much.

DEXTROSE THERAPY

Intravenous administration of dextrose is one of the most powerful therapeutic measures in the physician's armamentarium for the treatment of liver disease. It is all-important to maintain the glycogen content of the liver cell. It is possible that hyperglycemia inhibits neoglycogenesis and results in needed rest to the enzyme systems responsible, thus contributing to faster recovery. For this, several measures are suggested. If ascites is present, one should start with concentrations of 50% dextrose in volumes of 100 to 200 cc. daily, continuing until the output of fluids exceeds the intake. After this, administration of 300 to 400 cc. of aqueous 25% dextrose solution should be continued until there is another demonstrable increase in the output of fluid, when one may use 10% aqueous dextrose solutions in volumes of 3,000 to 4,000 cc. daily. If at any time during this regimen the output of fluids is less than the intake, one may have to resort as before to use of the more concentrated solutions to restore the fluid balance.

A difference of opinion exists, however, concerning the advantages of intravenous dextrose therapy if the patient can take the "necessary" dextrose or carbohydrate by mouth.[3] The "necessary" amount of carbohydrate is that amount sufficient to raise the blood sugar to a level that will suppress hepatic sugar output. However, while the normal liver will respond to the usual postprandial hyperglycemia, associated with a high carbohydrate intake, the "irritable" liver in patients with acute toxemia may require a much higher blood sugar concentration to inhibit gluconeogenesis. That this is so is seen in the prompt curtailment by the acutely poisoned liver of its output of sugar when large doses of dextrose are given intravenously, while small doses have little or no effect.[4] Furthermore, as Cori and Cori [5] have pointed out, for the normal liver "the blood sugar concentration and not the amount of glucose administered must be regarded as important for the rate of its glycogen deposition." Consequently, when an attempt is made to protect a damaged liver by means of glycogen deposition therein, the blood sugar concentration may have to be raised to a level impossible to obtain by ingestion of carbohydrates. In such cases, the intravenous infusion of dextrose is essential. The fact that extreme hyperglycemia so produced may result in glycosuria should not deter one from such vigorous therapy. Wakim and Mann [6] have shown that regeneration of hepatic tissue after injury begins in islands of normal cells that are supplied mainly by arterial blood, while the cells in areas supplied only by portal vein blood may be too badly injured to regenerate. If the cells from which regeneration is to originate are to receive the full benefit of high dextrose concentration so that they can begin to restore liver parenchyma, the hyperglycemia following intravenous therapy is desirable.

Because of the glycosuria that may result from intravenous dextrose therapy, some physicians favor the routine use of insulin with the sugar. However, unless the patient has diabetes, the indiscriminate use of insulin may defeat the purpose of dextrose administration. Soskin, Allweiss, and Cohn [7] have shown that, in the presence of sufficient insulin to maintain a normal constant blood sugar level, no additional insulin is necessary to obtain a normal hepatic response to administered sugar. The injection of insulin into the nondiabetic person can, therefore, produce no additional hepatic effect, but it does cause increased storage of glycogen in the muscles. This peripheral effect causes a fall in blood sugar, which in turn stimulates the liver to pour out more sugar. Thus, the liver is deprived of glycogen rather than the reverse. Maintaining the hyperglycemia in spite of the administered insulin will prevent this reversal in effect but will not be more beneficial than the administration of the same amount of sugar without insulin. Soskin, Allweiss, and Mirsky [8] have shown that the use of insulin with dextrose, as compared with the use of dextrose alone, in the treatment of toxic, nondiabetic animals shortens life. After prolonged treatment by intravenous dextrose injections designed to suppress the sugar-producing mechanism of the liver, that organ requires time to recover from the inhibition of dextrose formation, so that hypoglycemia may appear one to three hours after cessation of the infusion.[9] This should be anticipated and treated with small doses of carbohydrate by mouth or intravenously if necessary. Many patients with atrophic cirrhosis and associated ascites have been definitely relieved by the daily parenteral injection of hypertonic dextrose solution, which not only is a factor in liver repair but acts as a diuretic agent. However, in patients with prolonged, overwhelming changes of the liver, this treatment may not produce as striking results as in those with early disease.

USE OF AMINO ACIDS

If the patient is unable to eat a full diet, it may be well to administer infusions of amino acids in doses adequate to maintain the normal nitrogen balance. Eckhardt and associates [10] and Lewis and co-workers [11] have questioned that hydrolyzed proteins or amino acids can be utilized normally in the presence of liver damage that may impair the deamination capacity. Eckhardt and associates [10] demonstrated that 500 to 1,000 cc. of 10% amino acid solution administered intravenously each day over a period of one-half to one and one-half hours was metabolized and excreted by patients with diseased liver in a manner differing little from normal. It was further demonstrated that, when this solution was the only source of nitrogen and lipotropic substance, clinical improvement occurred. Lewis and associates [11] and Fagin and Zinn [12] have reported similar results. A possible slight decrease in urea formation and a slight decrease in the rate of amino acid disappearance was reported in cirrhotic patients. Amino acids administered intravenously rapidly are not well tolerated either by cirrhotic or by normal persons. Evidence suggests that reactions are no more frequent in one group than in the other. Frequent side-effects include flushing, nausea, and vomiting.

VITAMIN THERAPY

The role of vitamin therapy of chronic liver disease is not entirely clear at this time. While it has become almost routine to include supplementary administration of vitamin B complex in the management of cirrhosis of the liver, definite evidence for vitamin B deficiency in cirrhosis per se has not been demonstrated.[13] Such vitamin therapy may be expected to be of value only when specific deficiency exists. Moreover, certain theoretical considerations suggest possible damage from excessive use of vitamins. For example, the administration of nicotinic acid in large doses may be harmful in the presence of fatty liver (Chalmers and Davidson [14] and Handler and Dubin [15]). A portion of this vitamin is excreted as the methyl derivative. In animal experiments this has been shown to hasten the development of cirrhosis when a deficient diet was given. A possible antilipotropic effect has been implied.[15] McHenry [16] has suggested that thiamine hydrochloride therapy under certain circumstances may promote fat infiltration in the liver. Morgan [17] has deduced from experimental work that increasing the intake of nicotinic acid of persons with multiple vitamin deficiencies may precipitate conditions worse than the subacute deficiency state produced by an inadequately balanced diet. György [18] has pointed out that it is important to include adequate vitamin B complex in the diet but that imbalance among elements of the B group should be avoided. The deduction is that massive use of any one element of the vitamin B complex is likely to be of little benefit when no specific deficiency exists and may be harmful. Cautious and specific use is therefore necessary. The role of vitamin B_{12} and its possible interrelation with folic acid, choline, and methionine have not been sufficiently explored to permit definitive comment at this time. Vitamin C administration is of value in protecting against some hepatotoxins and is used therapeutically to protect some of the enzyme systems and improve resistance of the liver cells. Vitamin A deficiency is common in liver disease because of impaired absorption resulting from bile deficiency, from impaired conversion of carotene to vitamin A, and from fixation of vitamin A by areas of damaged liver parenchyma. Vitamin D absorption is also defective because of biliary deficiency.

To prevent these deficiencies and for possible protection against loss of glycogen from the liver, supplementary doses of these vitamins should be given to the patient. Dried yeast in divided doses, amounting to 30 to 50 gm. per day, or liquid concentrates of yeast are to be used when tolerated, especially in cases of cirrhosis. Citrus fruit juices, 250 to 360 cc. daily, should be used as a source of vitamin C. Vitamins A and D in doses of 5,000 and 1,000 I. U., respectively, given once or twice daily, are of definite value. The vitamin B furnished by the dried yeast may be supplemented parenterally with thiamine hydrochloride doses of 10 to 20 mg. and nicotinamide in doses of 50 to 100 mg., especially in cases of severe liver damage, when the patient should also receive liver extract orally, 30 cc. three times daily, or 3 to 5 cc. of crude extract parenterally, two or three times per week.

Associated with the decreased flow of bile into the intestine in jaundice is a deficient absorption of vitamin K; when the liver is damaged, there is also a decreased production of prothrombin independent of the absorption of vitamin K. Hypoprothrombinemia results from inadequate absorption or use of vitamin K and is responsible for much of the hemorrhagic tendency that is common in patients with liver disease. Capillary damage and formation of abnormal blood clots are also important factors in this hemorrhagic tendency; however, and it should be recognized that hemorrhage is not always associated with hypoprothrombinemia. Aggeler and Lucia,[19] nevertheless, suggested that it is advisable to administer vitamin K to all patients with liver disease or jaundice, regardless of the prothrombin or bleeding time. It is most important to prepare such patients well for operations; a dose of 10 mg. of vitamin K given parenterally on at least four days before operation and four days after operation is suggested as a good routine practice. Usually a dose of 5 to 10 mg. of vitamin K given parenterally or 5 to 10 mg. orally will bring the prothrombin time to a maximum in 24 hours, and the effect will persist for four days. When liver damage is so severe that there is little response to vitamin K therapy, an infusion of 500 cc. of undiluted plasma will usually correct the hypoprothrombinemia to well beyond the danger point (60% of normal).

Evidence by Meyer and Howard [20] showed that the oral administration of acetylsalicylate and sodium salicylate to human beings in daily doses of 20 to 80 grains (1.2 to 5.3 gm.) consistently produced hypoprothrombinemia and hypocoagulability of the blood. This may be prevented by administration of vitamin K with the salicylate. Hemorrhagic manifestations with acute rheumatic fever may, in some cases, be due to the administration of large doses of salicylates.

Similarly, Shapiro and associates [21] reported that in man, as in the rat, salicylate in adequate doses induces prothrombinopenia, which can be prevented by administration of vitamin K if liver function is adequate. Cirrhosis of the liver and preexisting hypoprothrombinemia augment the effect of salicylate. Acetylsalicylate appears to be more potent than sodium salicylate. The salicylates act, apparently, in the same way as bishydroxycoumarin (dicumarol®) but less effectively.

On the basis of this evidence, one might sound a note of warning as to the indiscriminate use of salicylates in diseases of the liver, particularly those associated with jaundice.

The subject of the so-called lipotropic agents, particularly choline and methionine, is still controversial. Perhaps at least part of the controversy surrounding the use of choline and its allies might be solved, as Best [22] has suggested, if lesions due to choline deficiency were distinguished from those due to other aspects of deranged liver function. If one agrees that the fatty liver is the primary evidence of choline deficiency, it should respond to appropriate therapy. So far as fatty changes occur in cirrhosis of the liver, particularly in the early stages of the process, the experimental evidence of Best and the suggestive clinical results of Morrison,[23] Steigmann,[24] Beams,[25] Beams and Endicott,[26] and Russakoff

and Blumberg [27] gave support to the effectiveness of choline and methionine. In spite of the results reported by Stevens and associates,[28] it remains a crucial question whether these agents are more effective than a diet of high protein and vitamin content. One well-controlled study [29] imputed to choline and methionine a definite protein anabolic effect beyond that produced by diets adequate in protein and vitamins in patients with chronic liver damage. The authors specifically pointed to an action of choline and methionine besides the lipotropic action. Fat accumulations were not present in biopsy specimens. Other authors have denied any protein anabolic action of choline and methionine. In a recent study of some interest Cornatzer and Cayer [30] advocated that patients be selected for choline therapy on the basis of an increase of phospholipid synthesis in response to a single large (10 gm.) dose of choline. Their conclusion was based on the finding (with radioactive phosphorus techniques) that in normal patients such medication does not alter phospholipid synthesis, while in cirrhotic subjects a significant increase can be demonstrated. In summary, choline and methionine seem to be of value when fatty infiltration exists as shown by biopsy or by clinical hepatic enlargement. These agents are of possible value in chronic liver disease because of a protein anabolic effect. However, this action is controversial, and even a lipotropic action beyond that found in a high protein diet has yet to be demonstrated beyond doubt. The best indication for the use of choline is a doubt as to the adequacy of protein intake in the presence of a fatty liver. Harmful effects of both cystine and methionine given in large doses have been reported,[29] and caution in their use is therefore advisable.

CIRRHOSIS ASSOCIATED WITH OTHER DISEASE

Fatty metamorphosis of the liver, associated with diabetes mellitus, has been treated with lipocaic. Evidence supporting this treatment is to be found in the observation of Fisher [31] and Allan and co-workers [32] that depancreatized dogs treated with sufficient insulin to control the diabetic symptoms show signs of hepatic insufficiency, become insulin sensitive and die in a state of hypoglycemia within one to eight months. Postmortem studies revealed a marked fatty infiltration and degeneration of the liver as the principal or sole abnormality. By the addition of raw pancreas to the diet, Allan and his co-workers were able to prevent such hepatic changes and to permit survival for a long time. Dragstedt, Van Prohaska, and Harms [33] prepared a fat-free alcoholic extract of beef pancreas (lipocaic) that, when fed to depancreatized dogs, proved as effective as raw pancreas, lecithin, or choline. They expressed the belief that it is a "fat-metabolizing hormone" concerned in the normal transport and utilization of fat. Dragstedt [34] administered lipocaic to patients manifesting diabetes mellitus in association with heptomegaly and noted a decrease in the size of the liver. Similar observations were made by Grayzel and Radwin [35] in three cases of juvenile diabetes mellitus treated with a pancreatic extract prepared according to the method of Dragstedt and his associates. Snell and Comfort [36] also reported a rapid decrease in the size of the liver and an improvement in the hepatic function during the first 12 days of lipocaic therapy. Rosenberg [37] observed recovery after treatment with lipocaic of a patient with fatty metamorphosis of the liver associated with diabetes mellitus. Biopsies were made before and after treatment, and results were correlated with those of liver function and dextrose tolerance tests, cholesterol determinations, and clinical course. The changes observed represented the clinical counterpart of the findings noted in experimental animals.

Crude aqueous liver extract, in addition to its lipotropic activity, seems to aid in detoxication and is definitely a part of the therapeutic regimen in cases of severe liver diseases. Its activity depends partially on its content of xanthine and partially on other, unknown, factors.

Another method of administering liver extract is the intravenous use of the water-soluble preparation. This has been advocated [13] for anorexic patients, in whom it has been claimed that it enhances the appetite and thus improves caloric intake. Ralli and associates [38] have reported a prominent increase in the five year survival rate of a group of patients treated by intravenous administration of 45 to 120 cc. of liver extract weekly, compared with a control group treated by diet, vitamin supplements, and liver extract intramuscularly.

Choline therapy in doses of 3 to 4 gm. per day may be of value when evidence of fatty infiltration can be demonstrated by biopsy of the liver or is seen clinically as enlargement of the liver.

An important symptom in liver disease that requires special attention is anemia, due in part to failure of absorption of iron because of the formation of iron soaps. Administration of iron salts, therefore, may not be successful in correcting hypochromic anemia caused by liver disease until the normal bile flow is restored. The macrocytic anemia seen with the severer liver damage is treated parenterally with liver extract but does not respond as well to this therapy as does pernicious anemia until the process causing the liver damage becomes quiescent.

Calcium deficiency is another defect in mineral metabolism associated with liver disease. This deficiency is caused by the lack of bile, resulting in impaired absorption of calcium and of vitamin D, and possibly by an excessive requirement for calcium when hepatotoxins are present. Calcium diminishes the hepatotoxic action of carbon tetrachloride and of certain other toxins. However, the experimental evidence for calcium therapy is controversial; that it can do no harm is evident; one may use it because occasionally a patient may be benefited.

For some time we have advocated the use of potassium iodide in cases of jaundice, because it seemed that the bilirubinemia disappears more rapidly after the use of this salt in doses of 10 to 20 grains (0.65 to 1.3 gm.) three times a day. If there is a syphilitic factor, the indication for the use of iodides is definite. The availability of penicillin for the treatment of visceral syphilis would naturally obviate treatment with arsenical or other heavy metal preparations in the presence of liver disease.

CORTICOTROPIN AND CORTISONE THERAPY

As in virtually all diseases in which definitive therapy is lacking, the effects of corticotropin (ACTH) therapy and cortisone therapy on cirrhosis of the liver have been explored. Aterman [39] has reported that hepatic fibrosis produced in experimental animals by administration of

carbon tetrachloride has been inhibited by cortisone simultaneously administered. A preliminary report of the use of cortisone in one case of biliary cirrhosis and one of serum hepatitis revealed no significant effect.[40] In a series of seven patients treated with corticotropin in daily doses of 50 to 100 mg. 6 to 28 days, no definite improvement was noted. There was suggestive improvement in albumin synthesis and a fall of bilirubin level in four young women with cirrhosis of unknown origin. Patients with Laennec's cirrhosis showed no improvement.[41] Serious complications occurred during corticotropin therapy. In three patients portal thrombosis developed, and in one a fatal esophageal hemorrhage occurred.[42] On the basis of this preliminary work, the use of corticotropin seems to be contraindicated in cases of advanced liver cirrhosis.

RETENTION OF FLUID AND SALT

The crucial factors leading to retention of fluid with ascites and edema in hepatic cirrhosis are not known. However, it seems that among the interrelated factors are portal hypertension,[2] increased sodium retention,[3] decreased colloid osmotic pressure of the blood, and[4] a possible increase in antidiuretic substance. Certainly reasonable doubt has been cast on the Starling principle that the volume of the extracellular extravascular fluid is dependent entirely on a balance between capillary hydrostatic filtration pressure and the colloid osmotic pressure of the blood.[43]

Although this factor plays a role, other factors also are involved. In patients with cirrhosis of the liver, accumulation of fluid and diuresis have occurred without alteration of the total protein and albumin levels.[44] Proof is lacking that albumin influences any aspect of cirrhosis other than fluid balance. Salt-poor human albumin has received extensive clinical trial for control of ascites and edema over the past few years.[45] Janeway and his associates [46] were the first to administer salt-poor albumin intravenously in the treatment of cirrhosis. Sufficient experience has accumulated in the literature to permit certain inferences at this time as to what may be expected from intravenous administration of salt-poor human albumin. The response in apparently similar cases is variable. In most series immediate and effective diuresis with loss of ascites and edema occurred in some cases. In others, response was slow over a period of weeks or months. In still others there was no benefit whatever. One group of workers [47] showed by electrophoretic studies a pronounced and immediate rise in albumin levels and a fall in globulin. After cessation of therapy this improvement gradually declined. In some reported instances,[48] elevations in serum albumin persisted for as long as three months after treatment. Maintenance doses of 20 to 100 gm. of salt-poor human albumin per week have been advocated.[43] The usual therapeutic dose has been 100 cc. of a 25% solution given intravenously in about 45 minutes one or two times a day. The duration of therapy depends on the response.

There is evidence [45] that a considerable part of administered serum albumin enters the ascitic fluid, establishing an equilibrium between the vascular and ascitic compartments at a higher albumin level. Albumin has been found more effective when the disease is not so advanced as to require paracentesis. However, when ascitic fluid exists in large amounts, it is economical of administered albumin to employ paracentesis prior to giving the intravenous medication. It is advisable also to restrict salt intake moderately to decrease the rate of ascites formation and thereby further conserve the serum albumin.[48] Salt-poor albumin has been most effective in treatment of the nutritional type of cirrhosis.[49] There are certain serious complications of intravenous albumin therapy (Post,[45] Watson and Greenberg,[50] Havens and Bluemle,[51] and Faloon and associates [49]). These include febrile reactions, hemorrhage from esophageal varices, epistaxis, formation of pleural effusion, and acute pulmonary edema. All these complications have been frequent enough to command caution, particularly in patients with known heart disease who have had previous episodes of hematemesis. Intravenous use of salt-poor human albumin is no substitute for nutritional and other recognized therapeutic measures for cirrhosis of the liver. However, when judiciously used in conjunction with other treatment, it may prove to be a valuable adjuvant in the therapy of decompensated hepatic cirrhosis with ascites and edema. In selected instances it may be of crucial benefit in enabling a patient to survive a critical period. Patients with cirrhosis of the liver and ascites with normal salt intake excrete minimal amounts of sodium in the urine in the order of 1 mEq. per day (Faloon and associates,[52] Farnsworth,[53] and Goodyer and co-workers [54]). Such patients may have decreased sodium content in the sweat and saliva also, indicating a possible adrenal mechanism in the sodium retention of cirrhosis with ascites (Bongiovanni and Eisenmenger [42] and Eisenmenger and associates [55]). Salt loads given to cirrhotic persons with a normal glomerular filtration rate and renal blood flow revealed impairment of excretion, suggesting a possible defect in the renal tubular mechanism.[54] However, the actual mechanism of the salt retention in cases of cirrhosis is not known at this time.

In view of the marked salt retention accompanying cirrhosis with ascites and edema, salt restriction techniques have been widely used in recent years. Salt deprivation has been attempted by dietary deletion and the use of sodium ion exchange resins. Layne and Schemm,[56] Kark and associates,[57] Lowe and Overy,[58] and Eisenmenger and associates [59] have claimed diuresis and a decrease in the rate of ascites formation as a result of diets low in sodium.

Such diets must be individualized for each patient. Kark and associates [60] recommended beginning with an intake of 25 mEq. of sodium per day and reducing or increasing this amount according to the response. A sodium intake that leads to diuresis in one patient may be ineffective in another.

Patients on prolonged salt restriction diets must be watched carefully for signs of the so-called low salt syndrome (Schroeder,[61] and Janeway and associates [46]). This is manifested clinically by weakness, lassitude, muscle cramps, nausea, and a drop in pulse pressure. If it is allowed to progress, the urea nitrogen level of the serum rises, and renal failure and death may occur. Serum electrolyte studies should be used to warn of a fall in the serum sodium level and changes in the carbon dioxide-combining power. The danger of this syndrome is partic-

ularly marked in patients with renal disease.[57] However, it may occur in cirrhotic patients with normal renal function.

Paracentesis entails less risk and may be resorted to frequently without greatly interfering with the general condition of the patient. Care must be taken not to withdraw too much fluid at one time or to withdraw it too quickly. Further, peritoneal shock should be prevented by carefully anesthetizing the peritoneum. Hypodermic solutions of atropine and epinephrine should be close at hand in case the patient suffers from the effects of peritoneal shock.

In patients whose salt intake has been restricted, abdominal paracentesis increases the danger of the salt depletion syndrome, presumably owing to the large loss of sodium in the ascitic contents. This sequence has been reported in two cases recently.[62] When a salt depletion syndrome occurs, the most effective treatment in our experience has been the intravenous administration of 5% solution of sodium chloride in an amount calculated to replace the specific sodium deficit in the extracellular compartment. This amount can be easily determined from the body weight and the serum sodium level.

In the enthusiasm for sodium restriction it is important not to compromise the therapeutic, caloric, and protein contents of the diet. Although this is difficult to guard against even when low sodium, high protein foods are used, diets maintaining proper balance can be prepared.[48] To further this end and to achieve a more palatable type of effective low sodium diet, ion exchange resins have been introduced in the treatment of cirrhosis (Goodyer and associates,[54] and McChesney and co-workers[63]). Dock has emphasized the value of cation exchange resins in the control of edematous states. Erwin and associates,[64] Martz and co-workers,[65] and Hay and Wood[66] have found that effective diuresis occurred and subsequent fluid retention was retarded in cirrhotic patients by the use of cation exchange resins. They recommended 45 to 60 gm. of resin daily in doses of 15 gm., so that the diet can contain 1 to 3 gm. of sodium per day. The resin used should be potassium, saturated so that there is no potassium deprivation, which can be a serious complication of cation exchange therapy. Ammonium chloride should not be given when an ammonium cation exchange resin is used, since this would increase the tendency to acidosis.[66] There are, however, limitations to the clinical utility of cation exchange resins, as has been recently stressed by Greenman and co-workers.[67] The in vivo efficiency of these resins is usually 1 mEq. of sodium per gram of resin. Since ordinary diets provide 100 to 300 mEq. of sodium daily, these agents, in the amounts recommended, 60 gm. per day, are obviously insufficient. Furthermore, when the dietary sodium is withheld, the efficiency of the resins decreases markedly. Both hydrogen and ammonium resins produce acidosis in addition to the deviation of sodium to stools, which can be considered a beneficial effect except in subjects with impaired renal function. Resins must be used cautiously in the presence of renal disease. As with any form of salt restriction, the danger of a low salt syndrome is present. The use of cation exchange resins has a limited place in certain instances of hepatic cirrhosis as an alternative to other methods of salt deprivation.

Mercurial diuretics may be used in treatment of liver disease. However, their effectiveness in severe chronic disease tends to be decreased after repeated use. This fact calls into play the other means of diuresis discussed earlier. When mercurial preparations are used in conjunction with salt depletion techniques, manifestations of the salt depletion syndrome must be watched for.

PORTAL HYPERTENSION

In addition to the many problems in the edema and ascites of liver disease just described, there is the mechanical problem of intrahepatic vascular obstruction and consequent portal hypertension. The problem of portal hypertension was classically delineated by Whipple[68] in 1945 and has recently been reviewed in an excellent article by Welch.[69] In 1945 Blakemore and Lord[70] outlined a feasible procedure for surgical treatment of portal hypertension. Since that time Rousselot,[71] Blakemore,[72] Linton,[73] and Gerbode and Holman[74] described the results following direct portacaval and splenorenal anastomosis. Results are better in patients with extrahepatic portal obstructions and in young persons whose liver damage is slight. In instances of cirrhosis, Blakemore[72] has stated that, while no one test of liver function is a valid criterion for the determination of a reasonable operative risk, the operation is hazardous when the serum albumin level is below 3 gm. per 100 cc. or when the sulfobromophthalein retention exceeds 35%. While cirrhosis may be the commonest cause of portal hypertension, there is no necessary correlation between the severity of the cirrhosis and the degree of portal hypertension or its manifestations. Hepatocellular dysfunction may be relatively slight in the face of prominent portal hypertension with its sequelae, hypersplenism, and hemorrhage from engorged esophageal veins. It is important to realize that these two complications of portal hypertension are the chief aspects in which improvement can be expected from operative intervention. Ascites is likely to be decreased, while liver function will not be improved. Sufficient time has not yet elapsed for definitive evaluation of the results of the operation. However, the portal decompressing procedures appear to be helpful in carefully selected cases in which manifestations of portal hypertension are marked in proportion to hepatocellular damage.

PHYSICAL ACTIVITY

Bed rest for patients with active liver disease is a cardinal therapeutic principle. It has recently received certain experimental support. Studies by Bradley[76] and Meyers[77] by venous catheterization and sulfobromophthalein clearance techniques have shown that the hepatic blood flow in cirrhotic patients is decreased or normal. Flow is decreased by standing[76] or by passive tilting of the patient to the upright position.[78] This work may offer theoretical confirmation of the clinical impression that early mobilization of patients convalescing from liver disease is detrimental. It is known that liver cells are particularly sensitive to oxygen deprivation. Decreased partial pressure of oxygen, as in high altitudes or in the presence of anemia, may cause fatty changes.[22a] Meyers[77] has shown that in the enlarged liver the hepatic arteriovenous oxygen difference varies inversely with the flow

under fasting and resting conditions to give normal splanchnic oxygen consumption. Sometimes, when the liver is small and cirrhotic, the oxygen difference is not great enough to compensate for the markedly decreased hepatic blood flow, and oxygen consumption, therefore, is below normal.[77] It may be inferred that activity would further embarrass such a patient by further reducing the already impaired hepatic blood flow. One might speculate as to the value of increasing the hemoglobin level or perhaps administering oxygen to such a patient.

DIETARY REGULATION

Dietary regulation is an essential part of the treatment of liver disease. An early return of normal eating habits is one of the most important factors in the improvement of liver function after the liver has been damaged. The food should be palatable and served in an appetizing fashion, and feedings should be given at frequent intervals. Nothing is so depressing to the patient as an ill-arranged tray. He has little desire for food, and one should use every psychological effort to encourage an added caloric intake. Ravdin and his associates [79] stated that a caloric intake in excess of basal requirements is most important in protecting the liver and aiding repair of liver damage. A high caloric, highly nutritious diet is the most important single aspect of the long-term management of chronic liver disease. Such a diet should contain at least 3,500 calories. The following diet is suggested:

Foods Allowed

Cereals:	One serving daily of any type cooked or prepared cereal, i. e., enriched cream of wheat,® farina,® oatmeal, and cornflakes. Avoid those containing large amounts of bran.
Bread:	Enriched white, cracked or honey wheat, whole wheat, or rye bread, melba toast, holland rusk, zweibach, or white crackers.
Cereal substitutes:	Rice, noodles, vermicelli, spaghetti, hominy, and macaroni; all to be plainly prepared without the addition of highly seasoned or rich sauces.
Soups:	Lean broths and vegetable milk soups.
Meat:	Two servings daily of very lean meat, i. e., lamb, veal, beef, liver, chicken, or turkey; to be broiled, boiled or roasted without additional fat. Remove all visible fat. No gravies or sauces, pork, or pork products, including bacon. Four-ounce cooked portion equals minimum serving; may use more.
Fish:	Lean fresh water fish, i. e., perch, pike, trout, bass, or whitefish; to be broiled, boiled, poached, or baked without additional fat. None to be fried.
Cheese:	Cottage, cream, mild American or Wisconsin brick cheese. No other kinds are to be used.
Eggs:	One or two eggs daily; may be either soft boiled, poached, shirred, or scrambled over water. None to be fried.
Vegetables:	At least three or four servings daily of any type cooked or raw vegetable with the exception of raw onions, radishes, cucumbers, or sauerkraut; all to be prepared without additional fat.
Potatoes:	Mashed, baked, or boiled potatoes. None to be fried.
Fruits:	At least three or four servings daily of any type canned, stewed, or fresh fruits. One fruit should be citrus, i. e., orange or grapefruit or the juice of either.
Desserts:	Fruit as above. Simple puddings, custard, jello,® simple cakes, and wafers.
Beverages:	Three or four glasses of milk daily; may use more. Coffee in moderation, tea, decaffeinized or cereal beverages (sanka,® kaffee hag,® postum®), fruit juices, and water.
Butter:	Three teaspoons or pats per day.
Condiments:	None to be used except salt.
Sweets:	Sugar, jelly, honey, and hard candies as desired.

Foods to Avoid

Fried foods, oils, salad dressings, nuts, and peanut butter; smoked, spiced, or tinned meats or fish; pork and pork products; gravies and sauces; pies, pastries, and chocolate; alcoholic and carbonated beverages; spices and condiments.

Avoid Tobacco

*Sample Menu for Hepatic Regimen**

Breakfast	
Fruit (any type)	1 serving or more
Cereal (any type except bran)	1 serving (½ cup)
Milk	1 glass, 6 oz.
Eggs (prepared any way except fried)	1 or 2
Toast	1 slice or more
Butter	1 teaspoon or pat
Jelly	1 tablespoon
Coffee	
Cream and sugar	
10 a. m.	
High Protein Beverage†	⅕ part of recipe
Luncheon	
Meat, fish, poultry, cheese or eggs	At least a 4-oz. cooked portion of meat, fish, or poultry, or 2 eggs, or large serving of cottage, cream, or American cheese.
Vegetable	1 serving (½ cup)
Salad, vegetable—no dressing	1 average salad
Bread	1 slice or more
Butter	1 teaspoon or pat
Jelly	1 tablespoon
Fruit (any type)	1 serving or more
Milk	1 glass, 6 oz.
3 p. m.	
High Protein Beverage	⅕ part of recipe
Dinner	
Meat, fish or poultry	At least a 4-oz. cooked portion
Potatoes (any way except fried)	1 average serving or more
Vegetable	1 serving (½ cup)
Salad, fruit or vegetable—no dressing	1 average salad
Bread	1 slice or more
Butter	1 teaspoon or pat
Jelly	1 tablespoon
Fruit (any type)	1 serving or more
Milk	1 glass, 6 oz.
Bedtime	
High Protein Beverage	⅕ part of recipe
Crackers	2 double or more

*Hepatic diet with starlac® feeding has the following approximate content: protein, 170; fat, 172; and carbohydrate, 357 (total calories, 3,656). Hepatic diet with protenum® feeding has the following approximate content: protein, 170; fat, 173; and carbohydrate, 353 (total calories, 3,649). Hepatic diet with protelac® feeding has the following approximate content: protein, 168; fat, 172; and carbohydrate, 329 (total calories, 3,536).

†High protein beverage: starlac® (product of the Borden Company), 6 tablespoons; milk, 1½ cups; cream (coffee), 1½ cups; sugar, 7 teaspoons; eggs, 3; and vanilla, 3 teaspoons. Beat eggs, sugar, vanilla, milk, and cream until well blended. Sprinkle starlac® over mixture. Beat until well mixed.

Recent studies by Chalmers and Davidson,[14] Jones and Volweiler,[80] and Patek [81] indicate that an optimal distribution of the caloric content includes protein elements to the amount of 1.5 to 2 gm. per kilogram of body weight per day. This gives some margin of safety over the amount usually allowed, which has been shown to support liver repair (Kimball and Chapple [82] and Kark and associates [57]). Protein is the most effective dietary agent in protecting the liver from damage and in promoting its repair.[81] Indeed, it has been argued [83] that, when dietary protein intake is adequate, little will be gained by supplemental amino acid or lipotropic therapy. This assertion will be alluded to later.

The carbohydrate fraction of the diet should also be as high as possible to supply the bulk of the caloric needs and to exert a protein-sparing influence.

The indictment of fat in the diet of patients with liver disease is not well supported in recent clinical literature (Chalmers and Davidson,[14] Jones and Volwiler,[80] and Patek [81]). While it is true that liver damage in the experimental animal has been produced by diets high in fat,[15] these diets were also deficient in protein elements. When protein intake is adequate, it is questionable whether a diet high in fat leads to liver damage.[84] Convincing clinical studies have shown that a diet of 3,500 calories that provides adequate protein may contain up to 175 gm. of fat and still be effective in the management of decompen-

sated liver cirrhosis. The pertinent point is that fat should not be restricted below the level needed to allow a palatable diet and thus the desired high caloric intake. In general, fats of vegetable or dairy origin are better tolerated than those from meat sources.

HEPATIC FAILURE, COMA, AND JAUNDICE

The patient with severe liver disease is in danger of hepatic failure and coma. Here intensive intravenous use of dextrose, salt-poor human albumin, protein hydrolysates, liver extract, blood transfusions, and plasma in judicious combinations may be lifesaving. Oxygen therapy is necessary with these measures, to combat the hepatotoxic effects of anoxemia. Oxygen is best given in an oxygen tent. The use of nasal catheters is contraindicated, because pressure necrosis from the rubber may result from a possible uremic state, which can form a part of the clinical picture. We have seen severe pharyngitis and erosions of the nose with subsequent bleeding follow the use of rubber tubes in the nose and mouth.

Of the complications that occur in cases of jaundice, acute hepatic insufficiency and hemorrhage are the most important. Jaundice in patients with cirrhosis of the liver may appear as a transitory, almost unnoticed, episode; yet it should be considered a serious sign. Bed rest is imperative and hospitalization is required in cirrhotic patients with jaundice.[85] Finally, the whole therapeutic approach to this problem should be controlled by repeated laboratory investigations, which would indicate the improvement, if any, that has taken place in the liver as the result of the treatment outlined. We cannot urge too strongly the need for a conservative and scientific approach to the treatment of jaundice. One should not be too eager to operate just because of the presence of bilirubinemia, and one should not delay operation in a patient with a definite surgical type of jaundice. There is no substitute for keen clinical judgment with respect to this disease.

After the jaundice has disappeared and definite clinical improvement has been noted in patients disabled by liver disease, ambulatory management should be continued for many months, until results of repeated liver function tests indicate restoration to normal. When this has been brought about, the patient should be warned against exposing himself to the factors that brought about the original condition. In spite of the recent emphasis on dietary deficiency in the genesis of cirrhosis,[9] there is no change in the traditional interdiction of the use of alcohol in the management of the disease.

SUMMARY

The incidence of cirrhosis is increasing. The use of sulfonamides and other hepatotoxic agents and the occurrence of serum homologous hepatitis and epidemic hepatitis of World War II may be partly responsible. Recognition of the cause of liver disease is necessary for effective therapy.

Patients should be at bed rest and preferably hospitalized. The decrease in hepatic blood flow of cirrhotic patients while standing offers theoretical confirmation of the clinical impression that early mobilization of these patients is detrimental. Bed rest is imperative during jaundice in cirrhotic patients. A high caloric, high protein diet is important in the long-term management of chronic liver disease. A diet of 3,500 calories is suggested.

Intravenous infusion of carbohydrates is desirable, in order to hasten the regeneration of liver parenchyma. In patients with atrophic cirrhosis and ascites, the use of hypertonic dextrose solution induces diuresis. Infusions of amino acids may be necessary in order to maintain normal nitrogen balance in patients unable to eat a full diet. Administration of whole blood or plasma may be beneficial when there is marked hypoproteinemia, anemia, or a hemorrhagic tendency.

While it has become almost routine to include supplementary administration of vitamin B complex to cirrhotic patients, definite evidence of deficiency in cirrhotics, per se, has not been demonstrated. Vitamin K should be administered regardless of prothrombin or bleeding time. Vitamin A and D in doses of 25,000 to 50,000 units, given one or two times daily, are of definite value. Choline and methionine seem to be of value when fatty infiltration of the liver exists, although this is controversial, and their action other than that found in a high protein diet has yet to be demonstrated beyond doubt. The use of crude aqueous liver extract seems to aid in detoxication and should be a part of the therapeutic regimen for patients with severe liver disease. Intravenous use of a water-soluble liver extract has been recommended for anorexic patients. We advocate use of potassium iodide in cases of jaundice. If syphilis is a causative factor, the indication for the iodide is definite.

Although the crucial factors leading to retention of fluid with ascites and edema in cirrhotic patients are not known, the employment of salt restriction and diuretics as well as salt-poor albumin is suggested; however, such use is not without certain dangers.

The value of the administration of cation exchange resins is limited, since the amount recommended, 60 gm. per day, is insufficient and larger doses are impractical. Patients on prolonged salt restriction must be watched carefully for signs of the low salt syndrome. Abdominal paracentesis increases this danger when preceded by severe salt restriction and the use of diuretics. On the basis of preliminary work, corticotropin (ACTH) therapy and cortisone therapy seem to be contraindicated in treatment of severe liver cirrhosis. Surgical treatment of portal hypertension has its best indications in patients with extrahepatic portal obstruction and is hazardous when there is a marked liver insufficiency.

Although the laboratory studies have become very important tools for the diagnosis and management of liver disease, they are more valuable when interpreted in the light of keen clinical observation.

104 S. Michigan Ave.

Workmen's Compensation Laws.—The first real contribution to industrial diseases of the skin was made by Ramazzini in the year 1700. His unexcelled description of the dermatoses of bakers, farmers, silk-workers, washer-women and others has won him the appellation of "father of industrial hygiene."

Appreciation of the importance of industrial diseases has been recent in this country, and compensation laws were not enacted until well into the 20th century. The Federal Government made the first provision for compensation of injured employees in 1908. In 1911 the state of Wisconsin established the first Workmen's Compensation Law. Since then all states have enacted legislation to deal with industrial injuries. Frank C. Combes, M.D., Dermatology Problems in Establishment of Workmen's Compensation Claims, *Compensation Medicine*, March-May, 1952.

TECHNIQUES AND INTERPRETATION OF ROUTINE BLOOD CULTURES

OBSERVATIONS IN FIVE THOUSAND CONSECUTIVE PATIENTS

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Blood cultures are often essential in the diagnosis and prognosis of disease. Frequently, however, the results obtained are difficult to interpret and correlate with the clinical state of the patient. Limitations and confusions resulting may be attributable to (1) contamination due to faulty technique in the drawing of blood or in laboratory procedures, (2) preconceived ideas of bacterial "nonpathogenicity," and (3) variations in techniques of blood culture.

Bacteria can be recovered from the blood stream during physiological states and under all pathological conditions from minimal local infections to septicemias. The significance of an organism recovered from the blood stream lies in its meeting certain basic criteria. This study was made in an attempt to correlate the clinical status and the laboratory findings in patients who have had blood drawn for cultures. Certain criteria to facilitate this correlation were established.

Arnold [1] experimentally produced frank bacteremia in dogs by introducing a highly acid chyme into the small intestine from the stomach. This resulted in increased permeability of the wall of the small intestine to bacteria. Arnold further demonstrated that certain physiological alterations in the body, such as adaptations to extremes of temperature, whether artificially induced or from disease, may result in bacteremia. Cirrincione and Francona,[2] also working on dogs, were able to confirm Arnold's findings.

Reith and Squier [3] reported a study of 293 subjects, of whom 278 were male, who had blood drawn for culture at random intervals while they were performing their usual daily occupations. All were subjected to a thorough physical examination, including dental x-rays. Bacterial growth resulted in 113 of the 293 cases. In 48 the bacteria were considered frank contaminants, while in 65 they were considered as being in the blood at the time of culture. An increase in positive blood cultures was noted during the months when upper respiratory tract infections were common, suggesting that they may, in part, be responsible for the rise.

Kulka [4] obtained positive blood cultures from apparently healthy women during menstruation, and Kobak,[5] using umbilical vessel blood cultures, confirmed the physiological entry of bacteria into the blood stream. The presence of bacteria in the blood during apparent health has resulted in studies on possible foci and primary sites from which the organisms invade the blood. Horder [6] as early as 1908 observed the "undoubted fact that the infective agent in most cases of subacute bacterial endocarditis was derived from the mouth." Libman [7] in 1918 reported that alpha streptococci were "constantly invading the blood from foci in the upper respiratory tract and oral cavities, even during periods of inactivity of the foci." Lewis and Grant [8] concluded that invasion of the blood stream is a common event in patients with diseased heart valves. They further state that such invasions are encountered in the great majority of cases without mishap and that an "almost physiological entry" of organisms into the blood stream of the average person constantly occurs. King,[9] in observations on 2,233 consecutive blood cultures, felt that "casual bacteremias" occurred rarely but, nevertheless, did occur.

Minimal trauma as a cause of bacteremia was demonstrated by Murray and Moosnick,[10] who obtained positive blood cultures from patients with chronic dental disease after they had chewed paraffin for one-half hour. Round and Kirkpatrick,[11] Burket and Burn,[12] and Okell and Elliott [13] all demonstrated bacteremia following intraoral manipulations. Hirsh [14] and his associates, using control studies, demonstrated the prophylactic value of penicillin in controlling such bacteremias. McEntegart and Porterfield [15] concluded that bacteremia following oral manipulations was related to the degree of trauma rather than to the intensity of oral sepsis.

Trauma, in the form of operative procedures on or about foci of infection, has repeatedly been observed to be followed by bacteremia. Seifert [16] reported that, 10 minutes after drainage of a variety of abscesses, positive blood cultures with organisms identical to those in the

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abscesses were obtained in 45% of his cases. Richards [17] demonstrated bacteremia following vigorous massage of foci of infection in 15% of 376 cases. Bacteremia, as one of the factors in radiation sickness, has been described by Warren [18] and Lawrence and Tennant.[19] Miller [20] and his associates have experimentally corroborated this observation.

Laboratory technique for blood cultures was different in every report reviewed. Extremes vary from single inoculation of one laboratory medium to fractionation of blood samples with inoculation of multiple mediums under both aerobic and anaerobic conditions. Skin preparation varied from simple alcohol swabbing to surgical preparation of the skin.

Variations in techniques, as well as differences in evaluation and clinical correlation of results of blood cultures, made an analysis of common factors in all references cited difficult. These differences, associated with the failure on the part of many workers to recognize the presence of bacteremia during various physiological conditions, emphasized the need for uniform methods of technique and interpretation of blood cultures.

Organisms recovered from blood cultures were used as the foundation for determining the correlation of bacteremia and the clinical state of the patient in this study. Bacteria whose pathogenic status is controversial, e. g., coagulase-negative Staphylococcus albus, diphtheroids, and Bacteroides, were given special study. The criteria established for interrelation of blood cultures reported here include (1) a consistent technique of sample drawing, (2) uniform methods of bacterial identification, (3) repeated cultures in series, and (4) compensation for complicating effects of chemotherapy and antibiotic therapy.

METHOD AND MATERIAL

Blood cultures of 5,000 consecutive patients, made at the Los Angeles County Hospital, Acute Unit, from Jan. 1, 1949, to Jan. 13, 1950, were reviewed. All blood cultures were routine. Clinical charts of all patients having positive blood cultures were reviewed, and bacteriologic-clinical relationships were analyzed and reviewed.

Five to 10 cc. of blood was obtained from the cubital vein through alcohol-prepared skin. The blood was inoculated into 6-oz. (170-gm.) medicine bottles through rubber-lined screw caps with central perforations. Mediums consisted of 100 cc. of DIFCO tryptose and phosphate broth with dextrose. A like amount of bile broth with dextrose was used for Salmonella, and 20 cc. of tryptose citrate broth was used for Brucella. To all mediums 1% paraaminobenzoic acid was added at the time of preparation as advised by Woods.[21] Penicillinase was added to the culture mediums from patients being treated with penicillin. All specimens were incubated at 37 C. Routine cultures were inspected daily the first week and semiweekly the second week. In the absence of growth, cultures were discarded at the end of the second week. Cultures for Brucella were placed in a 10% carbon dioxide environment after 48 hours. Every four to five days cultures were examined by smear. Subcultures were made the same time to tryptose agar slants, which were also incubated under carbon dioxide conditions. In the absence of growth in four weeks they were discarded as negative.

Relationship of Organisms Cultured to Concomitant Clinical States in 665 Patients

Organism	Bacterial Heart Disease	Pulmonary Tract Disease	Post Traumatic Sepsis	Upper Respiratory Tract Disease	Septicemia, Unknown Foci	Infantile Sepsis	Skin, Bone, Joint Disease	Genitourinary Tract Disease	Gastrointestinal Tract Disease	Group Totals A	Group Totals B
Group A *											
Staphylococcus aureus, coagulase positive	6	3	..	6	4	6	4	14	2	45	..
Beta streptococci	1	2	4	1	9	..	..	..	..	17	..
Nonhemolytic microaerophilic streptococcus	2	..	1	..	..	..	..	..	..	3	..
Proteus morgani	..	..	..	..	..	2	1	..	..	3	..
Proteus vulgaris	..	..	1	..	..	..	1	2	1	5	..
Salmonella	..	..	..	..	..	..	..	..	6	6	..
Diplococcus pneumoniae	..	110	..	..	..	..	..	..	..	110	..
Hemophilus influenzae §	..	..	..	..	..	..	..	..	..	6	..
Neisseria intracellularis §	..	..	..	..	..	..	..	..	..	7	..
Group B †											
Bacteroides	..	..	..	..	..	..	..	..	..	..	1
Clostridium welchii	..	..	..	..	..	..	..	..	..	..	1
Bacillus subtilis	..	..	..	..	..	..	..	..	..	..	17
Group A-B ‡											
Alpha streptococci	19	2	3	..	2	1	..	..	..	27	3
Nonhemolytic streptococci	9	..	2	2	..	1	..	..	..	14	4
Staphylococcus albus, coagulase negative	..	..	..	..	..	9	..	..	..	9	246
Diphtheroids	..	..	..	..	..	3	..	..	..	3	54
Escherichia coli	..	..	2	..	..	5	..	31	4	42	7
Pseudomonas aerugenosa	..	..	..	..	1	2	3	..	1	7	1
Aerobacter aerogenes	..	..	..	..	..	1	11	1	..	13	3
Alkaligines fecalis	..	..	..	..	..	4	2	..	..	6	2
Eberthella (nonspecific)	..	..	..	..	..	1	..	1	..	2	1
										325	349

* Positive bacterial clinical correlation. † Absence of bacterial clinical correlation.
‡ Classification dependent on clinical correlation in individual cases. § Organism produced specific associated clinical state.

17. Richards, J. H.: Bacteremia Following Irritation of Foci of Infection, J. A. M. A. **99**: 1496-1497 (Oct. 29) 1932.
18. Warren, S.: Pathologic Effects of Instantaneous Dose of Radiation, Cancer Research **6**: 449-453 (Sept.) 1946.
19. Lawrence, J. H., and Tennant, R.: Comparative Effects of Neutrons and X-rays on Whole Body, J. Exper. Med. **66**: 667-688 (Dec.) 1937.
20. Miller, C. P.; Hammond, C. W., and Tompkins, M.: The Incidence of Bacteremia in Mice Subjected to Total Body X-Radiation, Science **111**: 540-541 (May 19) 1950.
21. Woods, D. D.: The Relation of *p*-Aminobenzoic Acid to the Mechanism of Action of Sulphanilamide, Brit. J. Exper. Path. **21**: 74-90 (April) 1940.

RESULTS

Bacterial growth resulted in 665, or 13%, of the 5,000 cases reviewed. Approximately half (325) the organisms recovered in this study demonstrated bacteriologic-clinical correlation. Multiple invasion of the blood was demonstrated in 45 patients. Specific pathogenicity of the remaining half (340) was either indefinite or not thoroughly established.

On the basis of their probable etiological correlation with the diagnosis of the patient, organisms were placed into one of two groups, designated A and B. Bacteria were placed in group A if (1) an accepted etiological relationship between organism and disease existed, as in the case of meningococcemia and pneumococcemia, (2) repeated blood cultures grew organisms in which clinical correlation was probable, (3) disappearance of the organism from the blood paralleled clinical recovery, (4) bacteria recovered from the blood were identical with those recovered from foci of infection, and (5) in case of death, postmortem blood cultures corroborated the antemortem cultures. They were placed in group B if (1) organisms were obtained in only one of repeated blood cultures and in addition a specific etiological relationship was lacking, (2) the organisms, though potentially pathogenic, were not definitely related to the current illness of the patient, and (3) the organisms are accepted as being ubiquitous, e. g., Bacillus subtilis.

The accompanying table lists organisms on the basis of their grouping and their relationships to the clinical states of the patients. Organisms listed as belonging to group A with established pathogenicity need not be discussed in detail, as they fulfil the criteria for inclusion in group A. Organisms showing questionable pathogenicity are responsible for existing confusion and their status is in need of clarification.

COMMENT

The results of blood culture may be definitive in establishing a clinical diagnosis and determining the prognosis in any given case. Past clinical confusion in interpretaton has been dependent on the following factors: (1) unawareness of bacteremic states during apparent health and in association with minimal trauma, (2) preconceived ideas of certain "nonpathogenic" attributes of certain organisms, (3) disregard of special considerations of pediatric bacteriology, (4) lack of correlation with associated diseases in the host, (5) lack of standard technique of blood culture, and (6) failure to compensate for antibiotic and chemotherapeutic agents.

Bacterial invasion of the blood during health, during physiological alterations in the body, and during disease has been amply observed clinically and corroborated experimentally. Organisms recovered from the blood during health and after minimal trauma as reviewed in the introduction were considered to be chiefly and usually "nonpathogenic." The ability of these bacteria to multiply in the blood stream is usually low, and their power to produce a septicemic state is limited. Their presence is transient. These "nonpathogens," however, constitute a distinct threat to patients with chronic disease such as valvular heart disease. Loewe [22] and his associates, MacNeal and Blevins,[23] and McMillan [24] have demonstrated the role of oral alpha streptococci in the production of bacterial endocarditis.

Pediatric bacteriology as applied to blood culture requires special consideration. Organisms effectively overcome by adults can be both morbid and fatal to infants in spite of treatment. All the cases of Staph. albus, coagulase-negative, in group A were in cultures from pediatric patients. Gram-negative bacilli also demonstrated an increased pathogenicity in infants and children having limited immune mechanisms. An excellent opportunity for comparing antemortem and postmortem blood cultures was made possible by the high percentage of autopsies on the pediatric service. Blood culture results could be correlated in 20 of 27 cases. Of these, coliform bacilli were present alone or as part of a multiple invasion in 16 cases in sufficient numbers to indicate blood stream invasion in life. In instances of multiple invasion, so-called nonpathogens have been associated with disease production. Kanof and Kramer [25] reported 24 cases of multiple invasion in children; organisms usually considered spurious invaders were associated etiologically with the death of two.

The role of metabolic diseases and other associated disturbances in physiological processes affect the role of the host in resistance to bacteremia. A high incidence of diabetes and azotemia was observed among patients in whom facultative pathogens produced disease. Any alterations in immune response due to these factors require consideration.

Review of the literature showed a lack of comparable blood culture techniques. No correlation between the more elaborate methods of skin preparation and a decrease in contamination could be established. The time of obtaining the blood specimens for culture bore little relation to the incidence of positive cultures. The frequency in terms of times per day of obtaining blood for culture revealed no percentage difference of positive recovery attributable to the time factor. Multiple or complex mediums showed no increase in positive blood cultures.

Recent therapeutic advances have introduced new complications into blood culture studies. The use of para-aminobenzoic acid and penicillinase when indicated is fundamental.

An analysis of the diseases associated with blood stream invasion in this study emphasizes the importance of the above considerations. Except for B. subtilis, no organism can be considered as an invariable contaminant. Clostridium welchii and Bacteroides, though placed in group B exclusively, have been shown by numerous other studies to be capable of producing septicemia. Nine organisms are listed in group A-B. The so-called nonpathogens, such as Staph. albus and diphtheroids, fulfil the criteria set up for pathogenicity and in certain cases were considered of etiological signifi-

22. Loewe, L.; Plummer, N.; Niven, C. F., Jr., and Sherman, J. M.: Streptococcus s.b.e. in Subacute Bacterial Endocarditis, J. A. M. A. **130**: 257-260 (Feb. 2) 1946.

23. MacNeal, W. J., and Blevins, A.: Bacteriological Studies in Endocarditis, J. Bact. **49**: 603-610 (June) 1945.

24. McMillan, R. L.: Subacute Bacterial (Streptococcus Viridans) Endocarditis Treated with Penicillin, Am. J. Med. **1**: 628-633 (Dec.) 1946.

25. Kanof, A., and Kramer, B.: Multiple Invasion of the Blood Stream, J. Lab. & Clin. Med. **27**: 173-180 (Nov.) 1941.

cance. All organisms exclusive of B. subtilis placed in group B were not considered as contaminants, but rather their presence was accepted as being part of the large group of blood stream invaders during periods of physiological alteration, whatever the cause. Organisms in group B most frequently were associated with an initial positive blood culture followed by repeated negative ones. The failure to grow the organisms repeatedly may be explained by the institution of treatment immediately after the initial blood culture. Low virulence associated with their rapid destruction, along with the possibility of few circulating organisms, also may have contributed to their absence from subsequent blood cultures. Bacteriologic-clinical correlation was uniformly absent in cases in which group B organisms were grown.

SUMMARY

A review of blood cultures of 5,000 consecutive patients indicated the need for and resulted in the establishment of certain criteria for blood culture study, bacteriologic interpretation, and clinical correlation. These criteria included factors affecting the organism, the host, and therapeutic regimens.

Blood for culture was obtained through alcohol-prepared skin with no special considerations as to time of day or number of samples per day. Bacterial growth resulted in 665, or 13%, of the 5,000 cases reviewed. In 50% of the cases the organisms were classified in group A, indicating positive bacterial-clinical correlation in that they fulfilled the following criteria: (1) an accepted etiological relationship between organism and disease existed, as in the case of meningococcemia and pneumococcemia; (2) repeated blood cultures resulted in growth in which clinical correlation was probable; (3) disappearance of the organism from the blood paralleled clinical recovery; (4) bacteria recovered from the blood were identical with those recovered from foci of infection; and (5) in case of death, postmortem blood culture resulted in bacterial growth identical to that obtained in antemortem cultures. In the remaining 50% of the cases the organisms were classified in group B and were considered as "nonpathogenic" invaders because they (1) were obtained in only one of repeated blood cultures during the same disease and a specific etiological relationship was lacking; (2) though potentially pathogenic, were clinically unrelated to the current illness of the patient; and (3) are accepted as being invariable external contaminants, such as Bacillus subtilis.

The following organisms fitted into both groups in accordance with their roles in individual specific clinical states and as such may be classified as having pathogenic capabilities: alpha Streptococcus viridans, indifferent Streptococcus, indifferent micro-aerophilic Streptococcus, coagulase-negative Staphylococcus albus, Escherichia coli, Aerobacter aerogenes, Proteus vulgaris, Proteus morganii, Alkaligenes fecalis, Pseudomonas aeruginosa, nonspecific Eberthella, and diphtheroids. The recovery of organisms from blood culture in cases in which clinical-bacteriologic correlation is absent does not necessarily indicate laboratory contamination, but rather the possibility of bacteremia in association with physiological states or periods of physiological alteration, following both minimal and severe trauma, as well as during septicemic diseases.

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FACTORS INFLUENCING RUPTURE OF THE HEART AFTER MYOCARDIAL INFARCTION

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It is the purpose of this paper to review the factors related to the occurrence of rupture or perforation of the heart after myocardial infarction. Rupture of the heart has been recognized for over 300 years, and in recent times it has been the subject of thorough autopsy and clinical evaluation. The following salient facts have become established through previous investigations: 1. Such ruptures rarely occur in patients younger than 50 years of age.[1] 2. Patients who have unlimited activity after infarction occurs apparently have a higher incidence of rupture than those treated with "adequate" rest.[2] 3. Rupture associated with infarction almost universally occurs in the first few weeks following infarction; it rarely if ever occurs in an old scar.[3] 4. The chances of rupture occurring are three times greater in patients in whom hypertension persists after infarction than in those who have normal or subnormal blood pressures.[1a] 5. Myocardial necrosis is apparently a necessary prior condition for the occurrence of rupture.[4]

In an effort to find further information, we reviewed the records of 80 patients who died at the Los Angeles County Hospital between July, 1941, and October, 1951, of perforation of the heart with hemopericardium and cardiac tamponade. During this time there were, in addition, 11 patients who died from the effects of rupture of the interventricular septum following recent myocardial infarction. (Detailed analyses of the records of these 11 patients have not been included in this report.) Completed autopsy statistics are available at this hospital for the period July 1, 1941, to December 31, 1948, inclusive. In that period there were 13,665 autopsies; of these, 1,026 (7.58%) were performed on patients who died after recent myocardial infarction. Of this latter

Read before the Clinical Session of the American Medical Association, Los Angeles, Dec. 5, 1951.

Autopsy records were made available by Dr. E. M. Butt of the Department of Pathology, Los Angeles County Hospital.

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group, 73 patients, 7.11% of those with recent infarction and 0.53% of all patients on whom autopsies were done, died of cardiac rupture, either perforation through a free wall of the heart or perforation through the interventricular septum.

RESULTS OF REVIEW

The clinical, electrocardiographic (when available), and pathological records of these 80 patients were reviewed.

Clinical Records.—In both men and women the greatest incidence of rupture occurred in the seventh and eighth decades of life (table 1). None of the patients was less than 50 years of age. The average age of the men was 69.75 years and of the women, 72 years. The sex difference observed was striking: 33 patients (41.25%) were male and 47 (58.75%) were female. Regarding race, 79 were Caucasian and 1 was Negro.

Because of past emphasis on the fact that physical activity in the postinfarction period may be related to the incidence of rupture and because of recent articles relative to early activity in patients with infarction, the time of onset of infarction was carefully estimated from the history obtained in each case. The length of time from the estimated onset to entry into the hospital and the length of life from the time of estimated onset to rupture were calculated as carefully as possible.

The length of time from estimated clinical onset to entry into the hospital was as follows: 16 (20%) patients were in the hospital and in bed within 6 hours; another 9 (11.25%) entered between 7 and 12 hours after onset; 13 (16.25%) entered between 13 and 24 hours after onset. In addition, 11 patients (13.75%) were in the hospital at bed rest at the time of onset of the infarction. The remainder entered from 1 to 21 days after onset, 9 entering on the second day and 6 on the third day. Sixty-four patients (80%), therefore, either were already in the hospital at onset of infarction or entered within 72 hours afterward. Of the group entering later than that, several had been under the care of physicians at home or in private hospitals. Sex differences were apparent in this analysis: 17 men (51.5%) were admitted within 24 hours after onset of infarction, but only 20 women (42.7%) entered during the same period.

The length of life from estimated clinical onset to time of rupture was as follows: 14 (17.5%) patients died in less than 24 hours; 10 (12.5%) died on the second day; and 12 (15%) died on the third day; thus, a total of 36 (45%) patients died within the first 3 days of infarction. Another 27 (33.75%) died between the 4th and 12th days. In 11 instances, length of life after infarction was unknown, and in 6 instances, death occurred from 19 to 30 days after onset of infarction. Sex differences were found here also: 19 men (57.6%) and only 17 women (36.2%) died within the first 3 days.

Blood pressure observations, where available, were similar to those reported in the past.[1a] In cases in which preinfarction pressures were known, they were with few exceptions abnormally high. Following infarction, the pressure dropped to normal levels in a few cases, but the majority reflected either persistent hypertension or a drop to shock pressures.

The relation of digitalis therapy, causing increased myocardial contractility, to rupture of the heart has in the past been the subject of speculation.[1d] Ten (12.5%) of the patients reviewed had been receiving maintenance doses of digitalis, and 4 others were given digitalis in the last 2 to 4 days of life because of evidence of congestive failure. Thus, there is no concrete evidence to be derived from this series that suggests a significant relationship between digitalis administration and myocardial rupture. Similarly, quinidine sulfate, which was administered terminally to only 3 patients, cannot be implicated.

Electrocardiographic Records.—Electrocardiograms made in the recent antemortem period were available for 42 of the patients and for another 5 who died in the two year period 1939 to 1941. Electrocardiograms of 26 patients were made within 24 hours of death, those of 12 within 48 hours, of 4 within 72 hours, and of 5 within 96 hours. Records of four patients were made by the standard limb and multiple unipolar lead technique; records of three others were made by the standard limb leads plus multiple CF leads, and records of the remainder were made by the standard limb leads and lead CF_4.

TABLE 1.—*Distribution of Patients by Age, Sex, and Race*

Sex	Age, Yr.				Total	Average Age	Race	
	50-59	60-69	70-79	80-89			Caucasian	Negro
Men.....	4	11	15	3	33	69.75	33	0
Women.....	3	16	18	10	47	72	46	1

Nothing was found in tracings made by the standard and unipolar limb leads that could be correlated in any way with the later development of cardiac rupture. At best, these leads indicated only myocardial infarction. Chest lead tracings showed the following characteristics in patients with anterior wall and posterior wall perforation: 1. Anterior wall perforation—two patients in this group had multiple unipolar precordial leads, and in each, two or more positions showed QS waves characteristic of full-thickness myocardial infarction (fig. 1). In 2 subjects with multiple CF leads, QS waves appeared in two or more leads. A single lead, CF_4, was made in 30 patients; 20 of these had only QS complexes, 6 had deep Q waves, and 4 had essentially normal waves.

1. (*a*) Edmondson, H. A., and Hoxie, H. J.: Hypertension and Cardiac Rupture: Clinical and Pathologic Study of 72 Cases, in 13 of Which Rupture of Interventricular Septum Occurred, Am. Heart J. **24**: 719, 1942. (*b*) Friedman, S., and White, P. D.: Rupture of the Heart in Myocardial Infarction: Experience in a Large General Hospital, Ann. Int. Med. **21**: 778, 1944. (*c*) Zinn, W. J., and Cosby, R. S.: Myocardial Infarction: Statistical Analysis of 679 Autopsy-Proven Cases, Am. J. Med. **8**: 169, 1950. (*d*) Gans, R. H.: Acute Myocardial Infarction with Rupture of the Ventricle, Am. Heart J. **41**: 332, 1951. (*e*) Jetter, W. W., and White, P. D.: Rupture of the Heart in Patients in Mental Institutions, Ann. Int. Med. **21**: 783, 1944. (*f*) Segall, H. N.: Rupture of the Ventricular Myocardium: Report of 4 Cases with Comments on Pathogenesis and on Clinical Significance of Possibility of Cardiac Rupture in Prognosis of Coronary Artery Disease, Am. Heart J. **30**: 39, 1945.

2. Gans.[1d] Jetter and White.[1e]

3. (*a*) Footnote 1 *a*, *b*, *d*, and *f*. (*b*) Foster, L.: Spontaneous Rupture of the Heart: Clinical-Pathological Correlation with Presentation of 12 Cases, Quart. Bull., Northwestern Univ. M. School **20**: 209, 1946. (*c*) Krumbhaar, E. B., and Crowell, C.: Spontaneous Rupture of the Heart: Clinicopathologic Study Based on 22 Unpublished Cases and 632 from Literature, Am. J. M. Sc. **170**: 828, 1925. (*d*) Benson, R. L.; Hunter, W. C., and Manlove, C. H.: Spontaneous Rupture of the Heart: Report of 40 Cases in Portland, Oregon, Am. J. Path. **9**: 295, 1933.

4. Edmondson and Hoxie.[1a] Foster.[3b] Krumbhaar.[3c] Benson and others.[3d]

2. Posterior wall perforation—2 patients had unipolar precordial leads; in one there was a QS complex in lead V_6 (fig. 2), and in the other all precordial leads were normal. One patient had multiple CF leads, and a deep Q wave was found in leads CF_5 and CF_6. Of 10 patients examined with lead CF_4 only, 1 had a deep Q wave and the other 9 had normal QRS complexes.

Pathological Records.—The problem of pathological changes in the heart occurring after myocardial rupture has been extensively studied by competent pathologists.[5] In brief, the predominant changes apparently are extensive necrosis, undermining, and dissection of the myocardium. We have found no need to review the detailed histopathological condition of the hearts studied in our group, but we have attempted only to define the location of the infarct (table 2) and the location of the rupture

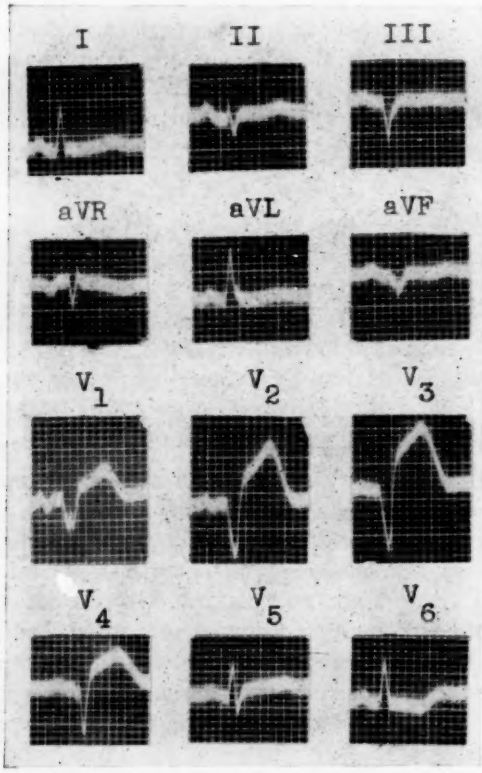

Fig. 1.—Electrocardiogram of patient with anterior myocardial rupture. Note the evidence of full-thickness infarction (QS waves) in leads V_1 through V_4.

(table 3) and then to determine if there is a predilection for any specific part of the heart to rupture.

In 77 (96.25%) patients, the infarcts were of the left ventricle, and in 3 they were of the right ventricle alone. In 11 (14.3%) of the 77 with infarction of the left ventricle, the infarction had spread to a portion of the right ventricle; in 46 (59.6%) the infarction was anterior, in 28 (36.4%) it was posterior, and in 3 (4%) it was lateral. Detailed subdivision of the locations of infarctions appears in table 2, but it may be noted that of the patients with anterior infarctions, the septum was involved in 31 (67.4%), and of those with posterior infarctions, the septum was involved in 17 (60.7%); of the entire group, therefore, the septum was involved in 50 patients (62.5%).

The distribution of the locations of ruptures is shown in table 3. Anterior left ventricle perforation occurred in 37 (46.25%) of the patients; in 31 (86.5%) of these, it was parallel to, in, or immediately adjacent to the interventricular septum. Posterior left ventricle perforation occurred in 25 (31.25%); in 16 (64%) of these, it was parallel to, in, or adjacent to the interventricular septum. In 9 the rupture was in the lateral left ventricle. In 7 it was through the right ventricle and was related to the interventricular septum. Multiple anterior perforations occurred in two instances, with specific locations of each perforation not given.

It is apparent, then, that in 54 (67.5%) of the entire group the rupture was parallel to, in, or immediately adjacent to the interventricular septum. It is also apparent that although the septum was actually involved in only 67.4% of those with anterior infarctions, in 86.5% of those with anterior ruptures the ruptures were intimately related to that structure.

TABLE 2.—*Location of Infarctions*

Location	No. of Patients
Left ventricle (total)	77
Anterior (total)	46
Entire anterior wall	5
Anterior wall and intraventricular septum	31
Anterior wall and septum	14
Anterior-apical and septum	12
Anterior, septum, and right ventricle	4
Anterior wall and basal septum	1
Anterior-basal	1
Anterior-lateral	6
Anterior-apical	1
Anterior-apical and lateral	1
Posterior (total)	28
Entire posterior wall	3
Posterior wall and intraventricular septum	17
Posterior-basal and septum	2
Midposterior wall and septum	2
Posterior, septum, and right ventricle	7
Posterior wall and septum, entire length of septum	4
Posterior-lateral and septum	2
Posterior-basal and posterior papillary muscle	1
Midposterior wall	2
Posterior-apical	2
Posterior-lateral	3
Lateral (total)	3
Right ventricle (total)	3
Anterior-apical and intraventricular septum	2
Apical-lateral	1
Total	80

In this entire group, the great majority of perforations were dissections, often by devious routes, from endocardium to pericardium. The length of dissection in each instance was variable; not only did blood dissect in a tortuous course through the ventricular wall in many cases, but in several instances the path was through the ventricular wall for several centimeters and then into the septum, parallel to the two septal surfaces, with final perforation into the pericardial cavity from the septum itself. The so-called blowout occurred in only a few instances, and in each of these it was through either the free lateral wall of the left ventricle or through an extensively necrotic anterior wall of the left ventricle.

5. (*a*) Edmondson and Hoxie.[5a] Krumbhaar and Crowell.[5c] Benson and others.[5d] (*b*) Snyder, G. A. C.: Spontaneous Double Rupture of the Heart, Arch. Path. **29**: 796 (June) 1940. (*c*) Lodge-Patch, I.: The Ageing of Cardiac Infarcts, and Its Influence on Cardiac Rupture, Brit. Heart J. **13**: 37, 1951.

COMMENT

Comparison of our data with figures obtained at an earlier period at the Los Angeles County Hospital by Edmondson and Hoxie [1a] shows that the increase in the number of patients with myocardial infarctions, about which they commented, has continued since the time of their study. Of all patients on whom autopsies were performed during the years they reviewed, 3.4% had one or more unhealed myocardial infarctions. Over twice that number (7.58%) were found in the same classification in the present study. The number of patients with rupture of the heart, however, was similar in the two series, with 8.3% in their group and 7.11% in ours. The generally accepted incidence in the accumulated literature is about 9%.[1d]

Age, Sex, and Race.—Our figures on age, sex, and race are worthy of further comment. Not one of our group, including the unreported series of 11 patients with interventricular septal perforation, was below the age of 50 years; by far the highest incidence for both sexes occurred between ages 60 and 80 years. On its face, this data apparently is good evidence that the clinician need

TABLE 3.—*Location of Ruptures*

Location		No. of Patients
Anterior left ventricle (total)		37
Parallel to, in, or near intraventricular septum	31	
Anterior-basal	1	
Anterior-lateral	2	
Anterior-apical	1	
Anterior, specific location not stated	2	
Posterior left ventricle (total)		25
Parallel to, in, or near intraventricular septum	16	
Posterior-basal	1	
Posterior-lateral	4	
Posterior-apical	1	
Posterior, specific location not stated	3	
Lateral left ventricle (total)		9
Midlateral	7	
Apical-lateral	2	
Right ventricle (total)		7
Anterior-apical, related to intraventricular septum	5	
Posterior-basal, adjacent to intraventricular septum	2	
Multiple anterior, specific location not stated (total)		2
Total		80

have little fear of cardiac rupture in patients below the age of 50 years. Regarding sex, women have an incidence of myocardial infarction in various autopsy and clinical studies only one-fourth [6] to one-seventh [7] as high as men. When considered in the light of sex differences, as revealed by an autopsy "population" study by Zinn and Cosby,[1c] the autopsy incidence is about equal for the two sexes. In our group of 80 patients with cardiac rupture, however, 47 (58.75%) were women and only 33 (41.25%) were men. This difference is certainly significant and indicates the greater danger that this complication holds for women than for men. Especially is this so if it is recalled that the peak incidence of myocardial infarction in women occurs at a later age than in men. As far as race is concerned, it has been shown in certain series that the Negro race has a lower incidence of infarction than the Caucasian in a given autopsy population. This is borne out in our series, only 1 of 80 patients being Negro.

Relation of Activity to Rupture.—Previous studies have shown that in certain instances there is a definite relation between the degree of activity after infarction and myocardial rupture. Because of the specialized classification of the patients considered in at least one such study,[1c] this problem was reevaluated. As has been noted above, 49 (61.25%) of the patients in our series were in the hospital and in bed either at the time of or within 24 hours after onset of infarction. It is difficult to conceive how the course of events in these patients could have been affected by activity. In addition, as mentioned earlier, several of the patients who entered relatively late in the postinfarction period had been in other hospitals or otherwise under the care of private physicians. If it is assumed that all or some of these patients were kept at rest before transfer to the Los Angeles County Hospital, then the available evidence suggests even more strongly that activity does not play an important role in the

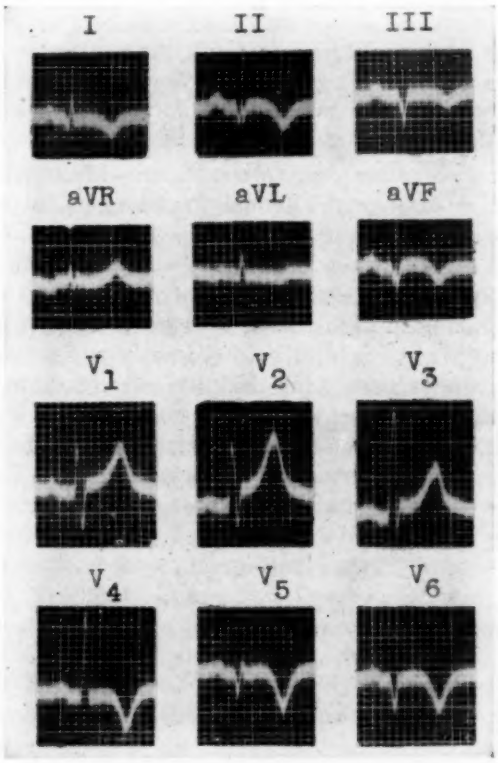

Fig. 2.—Electrocardiogram of patient with posterior myocardial rupture. Note that evidence of full-thickness infarction does not appear until lead V_6.

development of myocardial rupture. There may be exceptions in certain special instances or in cases in which activity has been actually excessive. That there may be a relation between activity and myocardial rupture, however, is possible. This is based on consideration of the fact that while 58.75% of the ruptures occurred in women, only 42.7% of the women entered the hospital during the first 24 hours. On the other hand, while only 41.25% of the perforations occurred in men, 51.5% of the men entered the hospital in the first 24 hours.

It has been stated repeatedly that the majority of deaths from myocardial rupture occur from the 2nd to

6. Clawson, B. J.: Incidence of Types of Heart Disease Among 30,265 Autopsies, with Special Reference to Age and Sex, Am. Heart J. 22: 607, 1941.

7. Parkinson, J., and Bedford, D. E.: Successive Changes in the Electrocardiogram After Cardiac Infarction (Coronary Thrombosis), Heart 14: 195, 1928.

the 10th day after infarction. Our figures do not differ greatly from these previously reported values. It is of interest, however, that in 36 (45%) patients rupture occurred within the first 72 hours; in 14 of these, in fact, it occurred within the first 24 hours, and in 10 within the second 24 hours. In one instance, a patient previously well reported for work, suddenly collapsed, and died. Several others were brought to the admitting room of the hospital because of severe chest pain and died at most only a few hours after onset of pain, before more than a cursory examination could be performed. On the other hand, rupture occurred after 19 days in 6 patients. At autopsy these patients had only the infarcts that had caused hospitalization; no evidence of more recent infarction was found. The maximum time after infarction of which we could be reasonably certain was 30 days. It is probably of significance that while approximately equal numbers of men and women died within the first 3 days (19 and 17, respectively), the percentage distribution was 57.6% men and 36.2% women. Men apparently are in greater jeopardy during the immediate postinfarction period.

Electrocardiographic Observations.—Myocardial necrosis is considered essential for development of the rupture, according to pathologists. If presently accepted electrocardiographic concepts are valid, semidirect leads over these areas should record only QS waves. The evidence obtained in this study appears to agree with that concept. In multiple precordial leads made in cases of anterior infarctions, a full-thickness infarct pattern (QS) was obtained at one or more areas. In cases in which a single lead, CF_4, was made, QS complexes were recorded in a majority of instances. In six patients with deep Q waves, lateral or medial displacement of the electrode theoretically would have revealed QS complexes. The ease with which the anterior and lateral portions of the heart may be explored electrocardiographically should enable the clinician to determine with a high degree of accuracy the extent of an infarction in those locations, both in thickness and in surface area involved. In our series, infarctions and ruptures were in anterior or lateral portions of the heart in 66.6% of the patients. In a recent survey of the literature [1d] it was shown that ruptures were anterior in 75% of 80 patients in whom the position of the rupture was reported. It would appear evident, then, that a clue to the possibility of impending rupture (i. e., a full-thickness infarct) may be elicited in two-thirds to three-fourths of the patients who will suffer this catastrophe.

The situation is somewhat different in the case of posterior rupture. Some evidence was obtained from lateral chest leads, but not with the same degree of certainty as in the case of anterior rupture. Esophageal or back leads would be of aid—the former if it were feasible to use these leads in critically ill patients, and the latter if they were in more general use and the criteria of normalcy were more definitely known.

Location of Infarcts and Ruptures.—It is well recognized that the majority of myocardial infarctions occur in the left ventricle. Wartman and Hellerstein [8] reviewed 235 infarcts in 160 patients. They found that the anterior half of the interventricular septum was involved in 54% of the patients who had an infarct of the anterior portion of the left ventricle. The posterior half of the septum was involved in 25% of posterior infarctions. Our series gives a somewhat distorted picture because of the fact that we considered only recent infarctions, although relatively few of the patients had old scars. Nevertheless, as noted earlier, 67.4% of anterior infarctions and 60.7% of posterior infarctions involved the septum. All infarctions in the right or left ventricle that involved the septum constituted 62.5% of the total. While percentage values based on such dissimilar series are difficult to compare, the extreme differences between them show that there tends to be a greater incidence of infarcts involving the septum in myocardial rupture than in those instances in which there is healing or death due to other causes.

Although loosely considered statistics may be fallacious, it is interesting to note that in 54 (67.5%) patients the perforations were intimately related to the septum. There appears to be a definite relationship between the number infarcts involving the septum and the affinity of perforations for the septum. Also, while the infarcts were confined solely to the right ventricle in only three patients, ruptures occurred in the right ventricle in seven. Finally, it is important to realize that few of the "ruptures" were actually ruptures in the sense of an area of heart muscle suddenly blown out of place. Almost all were dissections and perforations. This is generally true, also, of cases reported in the literature. No explanation is immediately apparent for this high percentage of infarcts and perforations that are intimately related to the interventricular septum. No explanation will be attempted here beyond consideration of a few possibilities. First, with the septum relatively fixed between the two ventricles, contraction may result in a tear along a line of "cleavage" between contracting myocardium and nonfunctioning necrotic tissues. Second, the initial tear through which blood later dissects may be related to the various muscle bundles of the heart and the ways in which they may work against or with each other during contraction.

Experimental work reported several years ago showed that intraventricular pressure apparently was not related to the development of rupture.[9] The large number of dissections, the small number of blowouts, and the fact that in 4 patients with both right and left ventricular infarctions the rupture occurred in the relatively low pressure right ventricle all suggest that only infrequently does intraventricular pressure alone play a significant role. Beyond some specific facts gleaned from a survey of autopsies, there is little we can state as to exactly why a given heart will rupture.

SUMMARY

1. Eighty patients who died in the period 1941 to 1951 of perforation of the myocardium with hemopericardium and cardiac tamponade have been reviewed. All of the

8. Wartman, W. B., and Hellerstein, H. K.: The Incidence of Heart Disease in 2,000 Consecutive Autopsies, Ann. Int. Med. 28: 41, 1948.

9. Thomas, W. C.: Clinicopathologic and Experimental Observations on the Pathogenesis of Rupture of the Heart Due to Myocardial Damage, Am. J. Path. 23: 904, 1947.

patients were over the age of 50 years. Women predominated over men (47 and 33, respectively). Only one of the group was Negro; the remainder were Caucasian.

2. Sixty-four (80%) of the patients were either in the hospital in bed or entered the hospital within the first 72 hours after infarction occurred. A higher percentage of men died within the first 72 hours than women (57.6% of the men and 36.2% of the women). Of all patients, 36 (45%) died within the first 72 hours of infarction.

3. Contrary to previous speculation, there was no evidence that digitalis administration was related to myocardial rupture.

4. Multiple unipolar lead electrocardiograms may give evidence of impending rupture by showing a full-thickness infarct pattern in anterior infarction in patients who otherwise fit the general clinical picture of those reviewed here.

5. The interventricular septum was involved in infarction in a greater number of these patients than could probably be expected in a random sampling of recent infarcts found at autopsy. Of the entire group, 67.5% had ruptures parallel to, in, or immediately adjacent to the interventricular septum.

6. The great majority of ruptures were dissections and perforations; only a few were "blowouts."

7. In general, with the exception that the amount of postinfarction activity these patients underwent did not appear significant, the results of the clinical survey did not differ considerably from the results of previous investigations referred to in the introduction.

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SPEECH REHABILITATION AFTER TOTAL REMOVAL OF LARYNX

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The problems that confront the patient who has undergone a radical laryngeal resection are generally not too well known. To present a total picture of the person who has undergone radical laryngectomy and his problems is one of the aims of this paper. Further, it is our purpose to show that practically all patients, after a total laryngectomy, can acquire a natural form of speech [1] without the use of any artificial aid and that they can resume their former occupations and activities requiring the use of the voice.

The number of patients with cancer of the larynx who have a total laryngectomy is increasing yearly.[2] They number in the thousands. Physicians in many communities in the United States and other countries now have to care for many more of these persons, whose medical needs are many, sometimes unique. The necessity for speech rehabilitation after the operation is now more widely recognized. Formerly it was believed that it was essential only to operate and save a life. Now it is realized that the laryngeal amputation is just the beginning and that the restoration of practical speech to the patient must follow.

After a radical laryngectomy the patient's entire economic and social status abruptly changes. Emotionally, a terrific blow has been sustained. He has been given a diagnosis of cancer; a serious operation and hospitalization follow; and immediately after the operation the patient is entirely speechless. The economic and other handicaps that will follow must be considered, for a radical readjustment of the patient's entire life is necessary. Only those dealing with large numbers of such patients can fill in the unhappy details.[3] Needless to say, the patient's discharge does not constitute the end of the case; it is just the beginning of the rehabilitation program that must follow.

The severest handicap that remains after the operation is the absence of speech. It is regrettable that patients are sometimes discharged without being informed that esophageal speech is a definite possibility. It is important that they be told this before the operation is started in order to prepare them emotionally for the postoperative and convalescent period. Patients are often discharged simply with a sheet of instructions on the use of the artificial voice box. Formerly, patients were dismissed without instructions of any kind in relation to speech therapy; however, this omission is fortunately becoming rarer. Surgeons who remove the larynx now assume the additional obligation of initiating a training program for their patients. The artificial mechanical devices should be reserved for the exceptional patient who cannot master esophageal speech for some special reason.[1] The mechanical larynx, aside from its other deficiencies, produces a tone that does not remotely resemble the human voice.

ALTERED ANATOMY AND PHYSIOLOGY AFTER THE OPERATION

Since esophageal speech depends on the remaining and altered anatomy and physiology, the more important changes following total laryngectomy will now be reviewed. After surgery the patient no longer inhales or exhales air through the nose and mouth. Only the esophagus connects with the mouth and nasopharynx, for the airway has been disconnected. A new orifice has been created in the neck where the tracheal stump has been sutured to the skin. Through this opening air is piped down into the lungs, and this air is sometimes exhaled with a noticeable hissing sound. The patient is now

1. Levin, N. M.: Teaching the Laryngectomized Patient to Talk (Without Aid of Mechanical Larynx), Arch. Otolaryng. **32**: 299 (Aug.) 1940; Teaching the Laryngectomized Patient to Talk, Year Book of the Eye, Ear, Nose and Throat, Chicago, The Year Book Publishers, Inc., 1940, p. 592.

2. Martin, H.: Incidence of Total Laryngectomy, Ann. Otol., Rhin. & Laryng. **59**: 359, 1950; Cancer of the Larynx in Nelson's Loose-Leaf Surgery, 1947 revision, New York, Thomas Nelson & Sons, chap. 5.

3. Levin,[1] Schall, L. A.: Psychology of Laryngectomized Patients, Arch. Otolaryng. **28**: 581 (Oct.) 1938. Mason, M.: Rehabilitation of Patients Following Surgical Removal of Larynx, J. Laryng. & Otol. **64**: 759, 1950.

speechless, and to many this sudden silence is terrifying, sometimes leading to an emotional depression. In order to make his wishes known, the patient who has undergone total laryngectomy must either resort to using a pad and pencil or use an ineffectual whispered speech. While swallowing remains a normal function after healing has

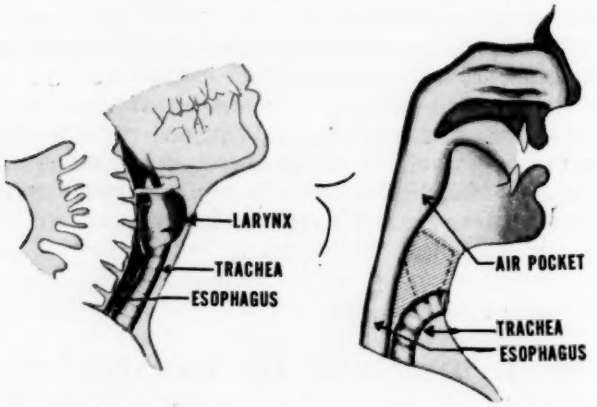

Fig. 1.—Left, normal anatomy, and right, altered anatomy after total laryngectomy, showing the permanent new tracheal opening (tracheostomy) into the respiratory tract. Only the esophagus now communicates with the nasopharynx and oropharynx.

taken place, it may often be accompanied by a gulping noise when the reconstructed hypopharynx is quite large. Occasionally the swallowing effort is difficult owing to esophageal stenosis resulting from a radical extirpation of an extensive malignant lesion. The person who has undergone total laryngectomy smells only the strongest odors, because after surgery he aspirates very little air through his nose. Later he learns to do this. Since olfaction is interfered with, taste is also altered. Those patients who are smokers find that it is nearly impossible to blow smoke through the nose for some time. Gargling, necessitating vocalization, is almost impossible, though later some are able to accomplish this.

After a total laryngectomy the tracheobronchial tree is in direct communication with the atmospheric air through the new orifice in the neck. Since the air is not previously warmed and moistened as in the preoperative state, tracheobronchitis is more prone to develop. The patient has in effect been deprived of the air conditioning system that formerly warmed, filtered, and moistened the air before it passed into his lungs. Now he inhales cold, hot, dusty, or dry air directly into the trachea. To this important physiological change he must also adjust himself. Sometimes a persistent and irritating cough will occur during the colder months, so that occasionally the patient must be sent to a warm climate during the first trying winter season.

With the removal of the larynx, other functions are lost. In addition to the production of vocal sounds, the larynx is involved in coughing, breathing, swallowing, expectoration, extreme muscular effort, and, finally, in the protection of the bronchi. After the operation all of these functions are either altered or lost. Coughing and breathing still continue through the tracheal opening in the neck. The discharge of excess quantities of mucus is sometimes very annoying. The protective action of the bronchi and the fixation of the chest on extreme muscular effort are lost. The most serious loss is, of course, the loss of voice. The voice is not regained spontaneously and must be acquired by reeducation and training in the great majority of cases. Other, less important results of the operation include: (1) absence of the epiglottis, which is often removed, since, if allowed to remain, it apparently serves no important function in the new speech mechanism; (2) failure of the pharynx to collapse (as in the normal state) and, sometimes, enlargement to such an extent that it resembles a diverticulum; (3) lowering of the base of the tongue, which may account for slight disturbances in swallowing.

SURGICAL ANATOMY AND TECHNIQUE

Since the hypopharynx and the upper esophagus are foremost in importance in the development of esophageal speech, laryngeal surgeons attempt to conserve as much normal tissue as possible, consistent with the removal of all the malignant lesion.[4] An effort is made to create an ample hypopharyngeal pouch, because a pharyngeal or upper esophageal stenosis is a serious complication in future speech training. The upper esophageal sphincter, with its striated fibers, is partly under voluntary control. If this structure has been preserved intact, it can be trained to take over efficiently the function of the substitute vocal cords. Efforts to artificially create membranous bands near the mouth of the esophagus, by plastic reconstruction, have been largely unsuccessful. It

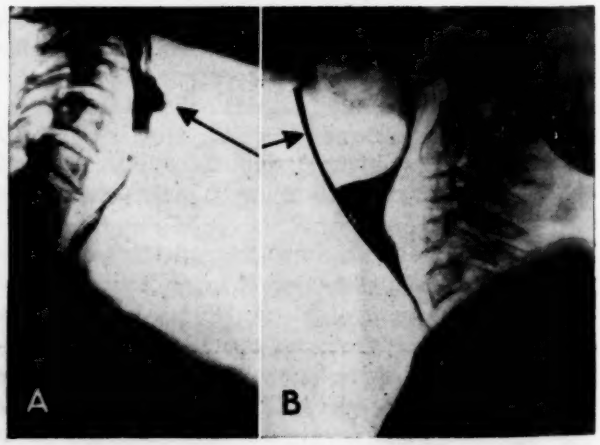

Fig. 2.—Esophageal speech mechanism, showing contrasting conditions. *A*, inadequate air pouch and stenotic pharynx, resulting from radical resection of an extensive tumor of the larynx and pharynx. The sphincter was also removed. *B*, an ample hypopharyngeal sac, satisfactory for development of esophageal speech.

is far better to preserve all possible normal tissue, particularly that of the esophageal orifice, together with its nerve and blood supply. There is still a need for technical modifications to facilitate postoperative speech development. My operative efforts now include more consideration for the anatomic structures that may favorably

4. (*a*) Levin.[1] (*b*) Jackson, C., and Jackson, C. L., editors: Diseases of the Nose, Throat and Ear, Including Bronchoscopy and Esophagoscopy, Philadelphia, W. B. Saunders Company, 1945. (*c*) Crowe, S. J., and Broyles, E. N.: Carcinoma of Larynx and Total Laryngectomy, Ann. Otol., Rhin. & Laryng. **47**: 875, 1938. (*d*) Jackson, C., and Babcock, W. W.: Laryngectomy for Carcinoma of the Larynx, S. Clin. North America **11**: 1207, 1931. (*e*) Babcock, W. W.: A Textbook of Surgery for Students and Physicians, ed. 2, Philadelphia, W. B. Saunders Company, 1935. (*f*) New, G. B.: Address of President: Carcinoma of Larynx: Methods of Treatment and Results, Tr. Am. Acad. Oph. **51**: 7, 1946. (*g*) Clerf, L. H.: Subglottic Carcinoma of Larynx, Pennsylvania M. J. **42**: 527, 1939. (*h*) Tucker, G.: Diagnosis and Treatment of Cancer of the Larynx, J. A. M. A. **149**: 119 (May 10) 1952.

affect future esophageal speech requirements. Further experience in this regard is needed.[5]

The mortality and morbidity rates incidental to a laryngectomy have been reduced to minimal figures. With the help of the antibiotics, sulfonamides, whole blood transfusions, good anesthesia, and nutritional in-

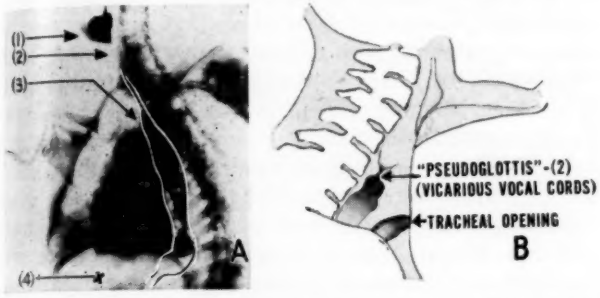

Fig. 3.—*A*, roentgenographic demonstration of esophageal speech mechanism (patient is saying "church"): (1) air-distended pharyngeal pouch; (2) vibrating upper esophageal sphincter, acting as substitute vocal cords (pseudoglottis); (3) air-distended esophagus; (4) gastric air, not ordinarily utilized in this speech mechanism. *B*, schematic representation of *A*, to show substitute vocal cords approximating at exact instant that a sound is produced.

travenous therapy, the period of hospitalization has been markedly reduced, from 8 to 12 weeks to 10 to 18 days. The total laryngectomy is recommended as the procedure of choice in selected cases of carcinoma of the larynx.[6] Additional radical neck dissection may be required in some cases. Five-year cures occur in 60% of the total number of patients operated on, many of whom live out their normal life spans. By contrast, deep x-ray therapy promises five-year cures in only 10% of patients.[6] Following radiation, there is, of course, no loss of speech.[7] The ideal procedure is the partial laryngectomy (laryngofissure), for it results in five-year cures in 75 to 85% of patients, without any serious impairment of speech.[8] Unfortunately, not too many qualify, for usually when the patient appears for biopsy, the growth has already extended beyond the scope of this operation.

MECHANISM OF ESOPHAGEAL SPEECH

The mechanism on which esophageal speech is based is fundamentally simple.[9] This mechanism utilizes structures that normally remain after the operation or that, if altered, can be trained to assume new functions. A comparison of the mechanisms of normal speech with those found in patients who have undergone total laryngectomy shows that the basic essentials for producing sound in both are the same. In each, a moving column of air from below vibrates closely approximated mucous membrane surfaces, thus producing a sound. The sound is then delivered into the mouth, where it is converted into words and sentences (speech) by the lips, teeth, tongue, and palate (the "molds of speech").

Esophageal speech differs from normal communication mainly in the anatomic structures involved. Normally, air from the lungs passes, on exhalation, up through the narrow aperture of the closely approximated and vibrating vocal cords (the glottis). In esophageal speech, the air pocketed in the upper esophagus passes upward through the closely approximated membranous surfaces of the vibrating cricopharyngeal sphincter (the pseudoglottis) into the hypopharynx. The sound thus produced is converted into speech by the "molds," which remain unaltered after surgery. I accomplished visualization of the substitute vocal cords in action, by radiography, in 1939.[1] It was clearly demonstrated that the folds of the cricopharyngeal sphincter approximated and vibrated at the exact moment that sound was produced and thus closely resembled the action of the true vocal cords on phonation. A column of air escaping through the vibrating sphincter constitutes the mechanism of sound production in esophageal speech. Normally this is also the mechanism that acts in belching. If this column of air can be controlled by prolonging the expulsion at will, the patient can then produce sounds that are converted into esophageal speech.[10]

It is neither a miracle nor a coincidence that air expelled from the upper alimentary tract can be used for producing sounds that can be converted into speech. In some animals and birds, sounds are normally produced by the use of anatomic structures other than the larynx. At times the upper esophageal sphincter must be removed to completely eliminate an extensive malignant lesion. In such cases other tissues may have to take over the function of substitute vocal cords in the hypopharynx. These tissues may be membranous or scar tissue folds, or combinations of these. The base of the tongue against the posterior pharyngeal wall, for example, can also be made to vibrate.

The upper alimentary tract offers a very satisfactory substitute for the respiratory tract in the new speech mechanism. The muscular cricopharyngeal sphincter is strategically situated at the mouth of the esophagus (pharyngoesophageal junction), approximately at the former level of the removed larynx. This muscular ring normally remains contracted and opens reflexly only during swallowing, vomiting, or belching. Since this sphincter also has striated fibers under voluntary control, it can be trained to act as a substitute for the vocal cords. The central nervous system still controls the speech mechanism, even though the larynx has been removed and the lungs are no longer necessary for speech production. The thorax still acts in a normal way, but on an inflated esophagus instead of on the air-filled lungs as in normal speech.[11]

The mechanism of esophageal speech in continuous action can best be described by a composite picture made up of repeated clinical observations on patients who have had total laryngectomy and by fluoroscopic and radiographic evidence.[12] The student begins to talk by closing his mouth, thus forcing air down into the pharynx, which

5. Levin.[1] Jackson.[4b] Sokolowsky, R. R.: Effect of Extrinsic Laryngeal Muscles on Voice Production, Arch. Otolaryng. **38**: 355 (Oct.) 1943. Crowe.[4c] Jackson.[4d] New.[4f]

6. Martin.[3] Jackson.[4b] New.[4f] Ward, G. E., and Hendrick, J. W.: Diagnosis and Treatment of Tumors of the Head and Neck: Not Including the Central Nervous System, Baltimore, the Williams & Wilkins Company, 1950, p. 597.

7. Kaplan, I. I.: Clinical Radiation Therapy, New York, Paul B. Hoeber, Inc., 1949, p. 340.

8. Jackson, C. L.: Voice After Direct Laryngoscopic Operations, Laryngofissure and Laryngectomy, Arch. Otolaryng. **31**: 23 (Jan.) 1940.

9. (*a*) Levin.[1] (*b*) Stetson, R. H.: Esophageal Speech for Any Laryngectomized Patient, Arch. Otolaryng. **26**: 132 (Aug.) 1937.

10. (*a*) Levin.[1] (*b*) Morrison, W.: Physical Rehabilitation of Laryngectomized Patient, Arch. Otolaryng. **34**: 1101 (Dec.) 1941. (*c*) Stetson.[9b]

11. Jackson.[4b]

12. (*a*) Levin.[1] (*b*) Stetson.[9b] (*c*) Lindsay, J. R.; Morgan, R. H., and Wepman, J. M.: Cricopharyngeus Muscle in Esophageal Speech, Laryngoscope **54**: 55, 1944.

becomes dilated; then the cricopharyngeal sphincter suddenly opens, permitting the air to go down into the esophagus. All this occurs with amazing rapidity. Immediately after the air is aspirated or swallowed, the esophagus dilates considerably. When the patient begins to make a sound, the air is forced upward, by a rising diaphragm, through the sphincter into the pharynx. The resulting sound is immediately converted into speech. As the patient gains facility by practicing the intake and subsequent expulsion of air, the act becomes much easier and faster. Later it becomes an involuntary reflex entirely. The gastric air pocket is not utilized in the speech mechanism of trained patients, a fact that is easily demonstrated by fluoroscopy or radiography.[13]

METHODS OF INSTRUCTION AND TRAINING

Formal instruction is necessary for most laryngectomy patients to acquire esophageal speech.[14] Occasionally a patient stumbles spontaneously into an excellent method by trial and error; however, learning need not depend on chance but can be directed by using methods that are known to be effective. Before a course of training is initiated, the patient must be examined to determine whether he is a suitable candidate. In the preliminary examination it must be established by fluoroscopy and radiography whether the hypopharyngeal pocket is ample and the upper esophageal sphincter functionally normal. At the same time the status of the respiratory function and the cardiovascular system is ascertained. The nose and throat are examined, and the hypopharynx and the esophageal mouth are inspected with a laryngeal mirror or, if necessary, an endoscope. A search is made for metastases, and the general health of the patient is considered.[1] Hearing must be adequate.

Preliminary orientation and training[15] may begin before the operation, whenever possible. After the operation the patient communicates by writing and is not permitted to attempt speech until the pharynx is completely healed. Whispered speech is ineffective, and it is prohibited because it interferes with the development of esophageal speech. Under ideal conditions, and as soon as the patient's physical condition permits, systematic training should begin. In addition to those patients who are regularly receiving speech instruction, convalescent patients and those scheduled for surgery may "sit in" during these classes. The psychological benefit for the latter is considerable.

A résumé of training methods used in successful speech rehabilitation[1] follows. 1. Patients are given an outline of the anatomic and physiological changes following the operation. They are taught that they must dissociate the separate functions of respiration through the tracheal orifice in the neck and aerophagia and phonation. Most patients grasp this idea readily. 2. Students begin to practice the aspiration and swallowing of air and its subsequent expulsion. Sipping carbonated liquids or water aids in the sensation of filling the hypopharyngeal pocket, because the effervescence helps in expelling this accumulation. 3. Using this expelled air, patients practice such easy words as church, scram, welsh, and others, and they are pleasantly surprised when these initial efforts result in clearly audible words. With the knowledge that they can now make themselves understood, there is considerable encouragement. 4. One-syllable words can readily be managed with one swallow of air; later, a sequence of syllables can be produced with an equal volume of air. 5. Combinations of various consonants with vowels are practiced, and, after the mastery of short words, words of more than one syllable are attempted. Long words are broken up into their component parts; thus, San Francisco becomes San-Fran-Cis-Co. 6. A series of short words are then combined into simple sentences, with the emphasis on clarity and sharp, clear diction. The intake of air is characterized by labored interruptions, as this is a deliberate, voluntary act. Later, the patient no longer consciously swallows or aspirates the air, as it has now become almost entirely a reflex habit.

Students are thoroughly drilled in each of the preceding steps for an hour daily. At the end of two weeks they can make nearly all of the fundamental sounds, say short words, and combine words into simple sentences. During the next three or four weeks the effort is directed toward polishing the speech and eliminating various defects, such as loud expiratory blowing sounds issuing from the tracheal orifice, gulping noises on swallowing air, unnatural lip movements, poor articulation, and others. Students can now practice three to four hours daily in interrupted periods.

Intelligence, willingness, and the determination to learn are essential requirements for the mastery of esophageal speech. Previous education is a help but not absolutely necessary. Some individual instruction is necessary, particularly in the initial and advanced periods of training. Beginners are much encouraged when they hear trained students talking. At the end of a month of instruction, the trainee usually talks quite well. His words are clear, and he is understood by almost everyone, although a few speech defects may remain. The patient is now ready for the test of talking to his friends and associates. Timid students are encouraged to listen to the new voice on a recording, so that they can appreciate the improvement and progress they have made. The hoarseness that characterizes early speech becomes less noticeable as students acquire greater facility and the voice more flexibility. Women learn to talk with the same ease as men. Persons who have undergone total laryngectomy generally present no unusual problems in training. Some however, have difficulties and peculiarities that require the experienced handling of a laryngologist who is also a teacher. The speech therapist should therefore consult with the surgeon to learn about the postoperative anatomic status of the difficult students. Some of this group have poor speech and show no progress in training, while others are using the mechanical devices unwillingly. These persons, of course, require special consideration.

Those who have accomplished esophageal speech come from all walks of life. We have trained salesmen, laborers, executives, engineers, society matrons, attorneys, housewives, a pharmacist, and others. Laryngectomy patients of all ages can be taught to master esophageal speech. The oldest student was well past 70,

13. Levin,[1] Morrison,[10b] Lindsay.[12c]
14. Levin,[1] Morrison.[10b]
15. McCall, J. W.: Preoperative Training for Development of Esophageal Voice in Laryngectomized Patients, Ann. Otol., Rhin. & Laryng. 52: 364, 1943.

and the youngest was 29. It is much easier to train patients if instruction begins shortly after the operation; however, patients have mastered this method after periods of months to years. One man learned to talk after a 22-year interval. Patients using mechanical devices can learn to talk and thus discontinue these artificial aids. The patient past 60 learns without too much difficulty if he has the desire to do so. Those who have a negative attitude or are depressed are at times difficult to train. Failures have been comparatively few, for those who could not acquire the method were either in ill health, depressed, or would not apply themselves sufficiently.

The patient who has mastered esophageal speech is able to talk distinctly in a normal way. The voice is satisfactory for normal speech activities and does not attract unusual attention, though it is somewhat harsh at first. A few patients develop voices so nearly normal that they are not recognized as laryngeal amputees, and their speech improves steadily over a number of years if correct methods are used.

ARTIFICIAL LARYNX AND OTHER MECHANICAL DEVICES

There are two common mechanical speech devices in use today: 1. The reed type of artificial larynx, which pipes air from the tracheal opening into the mouth, after a sound is produced by a vibrating reed. The resulting sound is then converted into a mechanical, artificial speech by the normal speech molds. 2. The electrolarynx, which is essentially a battery driven vibrator over which a diaphragm is stretched. This device is held against the neck. As the diaphragm vibrates, sound waves produced within the pharynx are delivered into the mouth and are articulated into a mechanical and muffled speech. The buzzing sounds resemble an electric razor in action.

Many of the patients who came for speech training were using artificial aids, but none was satisfied with them, even when they could use them successfully. All the patients were anxious to discard these mechanical prostheses, giving as the main objections and reasons that (1) they were conspicuous, attracting unwelcome attention; (2) they made the resulting voice unnatural and unpleasant, with a monotonous quality not resembling the human voice; and (3) they served as a constant reminder of the disability. Some patients who came for training had never used the artificial larynx, not having tried to master the artificial speech technique. Most patients were never informed that it takes as long to master these appliances as it does to acquire the more natural esophageal speech. Once speech is acquired, the aids are dispensed with in most instances. One patient preferred to use the instrument for telephone conversation only; another, a plant foreman, found that the artificial voice box carried well over the noises of machinery. An attorney who had been using the artificial larynx for 12 years was never reconciled to its use. He mastered esophageal speech in eight weeks, though his volume is still low because of the extremely radical neck, dissection procedure required in his case.

The artificial larynx is a poor substitute for a natural voice, and these mechanical devices should be reserved for only those few persons who cannot master esophageal speech for some special reason, such as (1) stenosis of the esophagus after extensive removal of a widespread malignant lesion; (2) resection of the cervical portion of the esophagus; (3) multiple handicaps; for example, laryngectomy plus deafness; (4) suspected recurrence, metastasis, or multiple lesions; for example, a bronchial carcinoma in addition to the laryngeal lesion; and (5) senility or other feebleness.

EMOTIONAL AND PSYCHOLOGICAL CONSIDERATIONS

Emotional disturbances of varying degree occur in nearly all of the patients.[3] While the introverted person suffers more in proportion, even the extrovert is depressed when he finds himself entirely speechless. These reactions are to be expected, because (1) the patient has undergone a major operation after confirmation of a serious diagnosis; (2) on discharge from the hospital he must return to his previous environment, with all of the economic and social problems involved, and where loss

Fig. 4.—Laryngectomy patient using reed-type artificial larynx. Patients find mechanical devices such as this objectionable, because (1) they are conspicuous and attract unwelcome attention; (2) the resulting voice is mechanical and monotonous; and (3) they require the constant use of at least one hand, thus are impractical for bimanual job requirements.

of speech is a serious defect; and (3) he has a fear of the recurrence of cancer, open or hidden, but definitely present. Formerly the patient faced the prospect of total laryngectomy with gloomy foreboding, the questions uppermost always being, "Will I survive?" and "What about my speech?" A hopeful answer can be justifiably given because of the five-year (and longer) cures that are on record.[16] Since the postlaryngectomy period requires major emotional and psychological adjustments, the chronically depressed type of person is not ordinarily recommended for this radical procedure without careful consideration.

REHABILITATION

Persons who have undergone total laryngectomy are located in many of the communities of the United States and other countries. Physicians who assume the care of these patients are very much interested in their unique and peculiar requirements. They must be supervised, instructed, and checked for a number of years. Certain

restrictions must be observed by these patients:[16] (1) They should not engage in occupations in which they will be constantly exposed to dust or irritating fumes and sprays. (2) Obviously they must use precaution while bathing and should keep out of deep water, since this is always an additional hazard. (3) They must guard against aspirating foreign bodies or debris through the vulnerable tracheal orifice. A gauze apron worn over the opening offers considerable protection against dust and wind. (4) Patients who wear trachea tubes must have these cleansed and changed regularly, and the tracheal orifice should be watched for irritation and recurrence of malignant disease.

The rehabilitation program for these patients should start preoperatively,[15] when they are assured that they can talk again. They are much encouraged when they hear others who have mastered esophageal speech, and they should be advised to enroll for a course of speech training promptly. This is by far the most constructive part of this program and the best morale booster. Insight into the total need of these patients came only with my integrated experience acquired in the combined roles of laryngologist, laryngeal surgeon, and speech teacher. My contact with this large group since 1932 convinces me that these patients are optimistic as to their present problems and their future outlook when they have proper aid in adjustment. The majority are able to resume their former occupations or other employment requiring the use of the voice, even over the telephone. Some have addressed groups in public and over the radio. Although several patients have come from neighboring countries for speech therapy, language differences did not present any real problems. Most of these rehabilitated patients have made admirable adjustment to their former lives.

Esophageal speech training has elicited a widespread interest among physicians, medical institutions, and university speech departments. The vocational rehabilitation divisions of several of the southern states have shown an active interest in salvaging these persons. They have adopted very practical programs and have helped to return many speech handicapped persons to gainful employment. One man who came for speech training had won an election as state senator, using an artificial device during the campaign. Even though successful, he was never reconciled to the use of this aid. He learned esophageal speech in about eight weeks, then discarded the aid. Now, intensely interested in the rehabilitation of persons like himself, he has been instrumental in effecting legislation that provides for subsidizing esophageal speech training in his state.

Pioneering work has established esophageal speech on a more solid foundation. Increasing interest is attracting laryngologists and speech pathologists to do more original work in this field, although there is still need for more cooperative effort in the interest of these handicapped persons. In addition to the training facilities now available, there is need for more active teaching programs, both for patients and teachers, in well-located centers.

SUMMARY AND CONCLUSIONS

A total picture of the patient who has undergone radical laryngectomy and his problems is presented. It is shown that nearly all these patients can return to occupations and activities requiring the use of the voice. The more important characteristics of the altered anatomy and physiology following this radical procedure are reviewed. While total loss of speech is most important, there are other marked changes that require consideration. The emotional and psychological disturbances following the operation are also considered.

Esophageal speech depends on certain anatomic structures, the most important of which are the hypopharynx and the upper esophageal sphincter. Laryngeal surgeons make every effort to conserve these and other normal structures that is consistent with adequate removal of the malignant tissue. The mechanism of esophageal speech is described. There is considerable interest in those structures that anatomically and physiologically take over the functions of the resected larynx. A résumé of successful methods of instruction used in esophageal speech training is outlined. The artificial larynx and other mechanical devices are discussed.

A rehabilitation program essential for these patients is outlined. The number of such patients is increasing yearly, because surgical techniques now assure from 50 to 60% of five-year cures (and longer), and many of them attain their normal life expectancy.

Patients can now be reasonably assured of a practical speech development after total laryngeal resection. Mechanical aids, with all of their deficiencies and disadvantages, are unsatisfactory and should be reserved for those few patients who cannot learn a more natural form of speech because of special difficulties. In short, the possibility of vocal loss should no longer deter the physician from considering the total laryngectomy operation as the procedure of choice when indicated. Esophageal speech adequately compensates for the loss of this important function.

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16. Levin,[3] Jackson,[4b] Crowe,[4c] Jackson,[4d] Clerf,[4g] Tucker.[4h]

Cleft Lip.—In newborn babies with cleft lip alone or combined with cleft palate, the first treatment of course is concerned with surgical closure of the lip. Regarding early treatment, it should be stated that cleft lip and cleft palate do not constitute a surgical emergency. Frequently, the physician who has delivered a baby with one or both of these anomalies is under the impression that immediate closure of the cleft is imperative to enable the baby to nurse, and that without surgical closure starvation is imminent. This is erroneous. The surest way to kill a baby in a poor condition of nutrition is to operate on it. No operation should be done until the child begins to gain weight and is otherwise in good physical condition. By the use of a little ingenuity, feeding can be carried on by medicine dropper, spoon or special feeders. Swallowing is greatly facilitated by holding the baby during feeding in the upright position. Some surgeons, prompted possibly by the natural anxiety of the parents to have the deformity masked as soon as possible, advocate operation on the lip within a few days after birth. We do not subscribe to this, as we feel that accurate coaptation of the cleft edges is more difficult when the parts are so small and that much better end-results are obtained by waiting until the child is six weeks to three months old.—Robert H. Ivy, M.D., Modern Concept of Cleft Lip and Cleft Palate Management, *Plastic and Reconstructive Surgery*, February, 1952.

GENITOURINARY LESIONS IN LEPROSY

WITH SPECIAL REFERENCE TO THE PROBLEM OF ATROPHY OF THE TESTES

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and
Lawrence L. Swan, M.D., New Orleans

Genitourinary lesions specifically related to leprosy (Hansen's disease) are relatively few. Of considerable clinical interest and importance are the frequent leprous orchitis, testicular atrophy, and gynecomastia. A review of urologic literature reveals no reference to involvement of organs of the genitourinary tract by the Mycobacterium leprae. Of the standard urologic textbooks only Young's [1] refers to leprous orchitis.

In the general literature of leprosy only passing reference is made to the genitourinary manifestations. Fox and Knott [2] described cutaneous leprous nodules on the scrotum and penis in 4 of 34 male patients. Serra [3] examined 200 patients with leprosy, describing vulvar lesions in 13%, preputial lesions in 10%, and lesions of the balanic sulcus in 5%. These lesions were especially common in patients with the nodular and mixed types of leprosy, although it is known that macular leprosy of the penis and vulva often mimics primary chancre. One patient presented a nodular lesion at the balanopreputial sulcus following intercourse with a woman known to have leprosy. Inguinal lymphadenopathy developed, and Myco. leprae were found on microscopic examination.

The diagnostician must be particularly wary in many cases, for two surveys conducted by the United States Public Health Service revealed that in presumably nonsyphilitic leprous patients there were 45% to 59% false positive serologic reactions for syphilis.[4] In fact, it has been estimated that approximately half of the patients admitted to the National Leprosarium at Carville, La., have had a diagnosis of syphilis made sometime prior to admission.[5]

In Serra's group of 200 patients with leprosy, testis and epididymal involvement was described in 97% and 29%, respectively. Bacilli have been described in the epididymis and in the rete testis, and Kobayashi [6] has even described bacilli in the seminal ejaculum. In a series of 842 patients with leprosy Baptista [7] described gynecomastia in 72 (8.6%). In another group of 292, gynecomastia was observed in 17 (5.8%).

While the kidney and more rarely the adrenal are frequently involved in a nonspecific type of amyloidosis similar to that seen in other degenerative diseases, no significant renal or adrenal lesion characteristic of leprosy has been described. Nephritis has been a frequent finding. The degree of renal and adrenal amyloidosis is often pronounced, and in large areas of many kidney sections the glomeruli are almost completely obliterated by amyloid. The adrenals are less commonly infiltrated by amyloid. Ureteral, bladder, or prostatic involvement by any process peculiar to leprosy has not been recorded to the best of our knowledge.[8]

It is the problem of leprous orchitis and atrophy that forms the basis for this preliminary report, in which a few of the clinical findings are correlated with the histological changes observed in the testis.

MATERIAL AND METHODS

One hundred seventy-nine male patients of the United States Public Health Service Hospital, Carville, La., were examined. In 154, only the breasts and testes were observed. In 25, more detailed examinations were carried out, including high-span and caliper testis measurements. In addition, notation was made concerning beard growth, voice changes, thyroid cartilage size, ejaculation, impotence, temporal recession of hair, trunk and axillary hair, pubic hair, and external genitalia. When it became apparent that height-span measurements were not indicative of an eunuchoidal skeletal structure, sole to symphysis pubis and symphysis pubis to vertex measurements were not made.

Formal biopsy specimens of the testis were obtained from three patients, two of whom had gynecomastia. Breast material was available from one of those who had previously undergone mammoplasty. Sections of breast were typical of classical gynecomastia, so that further studies with relation to the gynecomastia were not emphasized.

In addition to biopsy sections of the testis, tissue obtained post mortem from 17 patients with lepromatous leprosy was fixed in formaldehyde (formalin®) for study. Microscopic sections of the testes were stained with hematoxylin and eosin and for acid-fast organisms. Selected sections of testes were stained with Masson's trichrome and congo red. Urinary 17-ketosteroids and gonadotropins were determined in two patients subjected to testis biopsy.[9]

PATHOLOGICAL CHANGES

In every patient examined there was definite microscopic evidence of severe involvement of the testis. The histological changes varied markedly; these changes have been arbitrarily divided into three phases: (1) vascular, (2) interstitial, and (3) obliterative.

Read before the U. S. Public Health Service Clinical Society, Detroit, June 7, 1952.

Chief of Urological Service, U. S. Public Health Service Hospital, Norfolk, Va. (Dr. Grabstald); Chief of Pathology Service, U. S. Public Health Service Hospital, New Orleans (Dr. Swan).

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Vascular Phase (Active Leprous Orchitis).—The major changes during this phase are vascular. The vessels of all sizes are infiltrated by lymphocytes. The width of the vessel wall is increased at the expense of the lumen (fig. 1), and lepromas are occasionally seen as nodules projecting into the lumen. Perivascularly, in the interstitial tissues, there are numerous lymphocytes, large pale cells, and vacuoles measuring up to 40 μ. Acid-fast organisms are present in impressive numbers (fig. 2). Many of the vacuoles seen with the hematoxylin and eosin stain are globi containing packets of Myco. leprae, and the large pale cells have many bacteria contained within their cytoplasm. These are the lepra, or Virchow, cells. Acid-fast bacilli are also present in the vessel walls and globi, and lepra cells are observed in the interluminal lepromas. There are all phases of spermatogenesis during this stage. The Sertoli cells and the interstitial cells of Leydig are not affected. The basement membrane and lamina propria of the tubules are not changed.

Fig. 1.—Lymphocytic infiltration of artery immediately adjacent to the tunica albuginia. There is widening of the arteriole wall and perivascular lymphocytic infiltration (hematoxylin and eosin × 83).

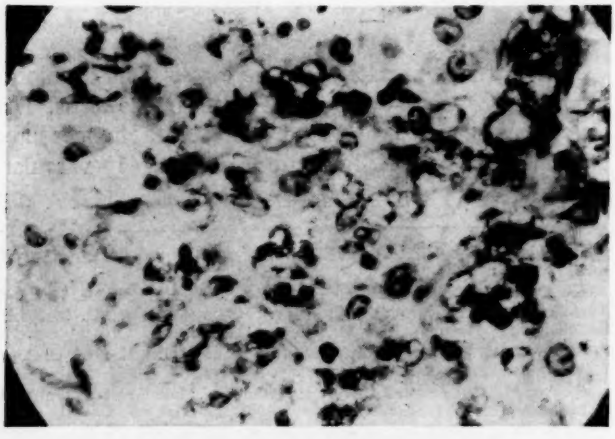

Fig. 2.—Acute leprous orchitis; acid-fast preparation showing typical organisms (× 430).

Interstitial Cell Phase.—Gradations into this phase are gradual, showing progressive reactive obliterative endarteritis, but the major findings consist of masses of Leydig cell clumps and interstitial fibrosis (fig. 3). The vessel walls are moderately to greatly thickened but lack any evidence of active inflammation as described in the preceding phase. The interstitial tissues show diffuse collagen deposition, with aggregates of Leydig cells. These cells appear to be larger, more eosinophilic, and granular than normal. There are numerous coarse brown granules in the cytoplasm in the so-called ectoplasmic zones of many cells. Crystalloid forms have not been observed within the cytoplasm. The seminiferous tubules are seen to be relatively smaller. The lumens are almost entirely filled with Sertolian syncytium. Occasionally spermatogonia are seen, but no mature spermatozoa are found. The basement membrane is wider than normal, and the lamina propria is considerably widened by concentric lamellae of delicate fibrous tissue. Acid-fast stains show considerable variation in the number of organisms at this stage. When they are present, globi are less frequently seen than in the preceding stage. These are present in the interstitial tissues in close relationship to the interstitial capillaries.

Obliterative Phase.—Again all degrees of gradation can be seen from the preceding phase to this final picture of complete fibrosis. Every microscopic field examined reveals the normal pattern to be replaced by a homogeneous fibrosis (fig. 4). No outline of seminiferous tubules can be detected, and vascularity is greatly diminished and almost limited to very small capillary-sized vessels. Acid-fast organisms, globi, and lymphocytes are almost uniformly absent.

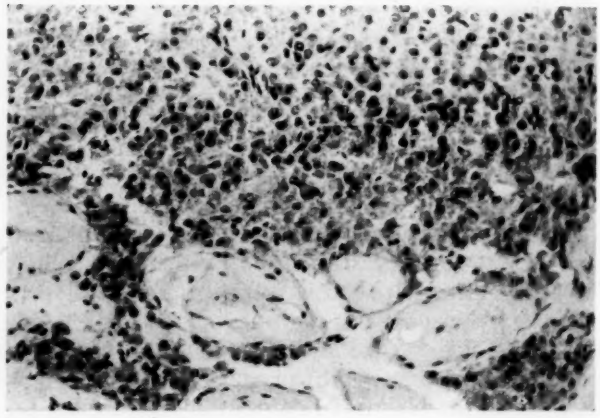

Fig. 3.—Aggregations of Leydig cells and atrophic seminiferous tubules in which a few Sertoli cells may be seen; acid-fast stain is negative (hematoxylin and eosin × 83).

Special stains of testis, epididymis, and ductus deferens for amyloid have been uniformly negative despite the fact that renal, adrenal, hepatic, and splenic amyloidosis is found in 65% of male patients studied postmortem. It appears that there is minimal vascular involvement of the epididymis during the bacteremia. Organisms, lymphocytic infiltration, and fibrosis of a lesser degree than in the testis are present in the epididymis. Giant cells, described by Young as being characteristic of leprous orchitis, have not been observed in our series.

PATHOGENESIS

Several features of the pathological picture are enigmatic. However, it can be stated with certainty that there is some degree of orchitis, or its residuals, in every male patient examined postmortem in this laboratory. At present it is difficult to correlate degree of atrophy with the age of the patient, or with duration or severity of disease.

It is remarkable that in leprosy the testis is so frequently involved and that in no other infectious disease process is there a quite comparable testis specificity. Obviously inherent physiological characteristics of the gonads or common embryological ancestry of the organs is of no significance, for the ovaries are not involved in

Fig. 4.—Complete fibrosis of testis; acid-fast stains negative (hematoxylin and eosin × 150).

any female patients studied postmortem in our series. It may be postulated that the environmental temperature difference between testis and ovary may account for this finding.

The pathogenesis of leprous orchitis and final atrophy appears to be a transition from an active, acute lepromatous orchitis to a final picture of complete atrophy of the testis with obliteration of all landmarks by fibrous tissue. It is presumed that the initial lesion is infiltration of the vessel walls and adjacent tissue by Myco. leprae. There is a concomitant lymphocytic reaction, and large numbers of acid-fast organisms are seen. The bacteria are present in typical aggregates as elsewhere in the body. Next is seen a focal and, finally, a complete disappearance of germinal cells, with replacement by a syncytium of Sertoli cells, which completely fill the lumens.

The interstitial tissues appear to be next involved. There is often rather striking clumping of interstitial cells. It is doubtful that there is a true interstitial cell hyperplasia. Myco. leprae have not been demonstrated during this stage. Apparently, by a process of fibrosis, the final phase is a complete disappearance of Leydig cells and seminiferous tubules, with terminal obliterating endarteritis. It has been observed in our group that adrenal amyloidosis is found in all subjects whose testes exhibited interstitial cells in larger than normal numbers. The exact significance of this is not known.

CLINICAL FINDINGS

The duration of known leprosy in these patients, whose ages were between 17 and 79 years, was six months to 50 years. Of 50 testes measured in 25 patients, 14 (28%) were atrophic on the basis of measurements below 3.0 by 2.0 cm. (normal, 4.5 by 2.5 to 3.5 by 2.0 cm.). It has been observed that atrophy is almost always bilateral. In many instances the presence of rather large hydroceles, which is not unusual in this group of patients, has made it difficult to obtain accurate measurements. It has been our impression that testis atrophy is far commoner in patients with the lepromatous type than in those with the tuberculoid type of leprosy. Gynecomastia was present in 32 of 179 patients (19%) (fig. 5). It is obvious that many patients observed to have testis atrophy had no gynecomastia. In only one patient was the height-span measurement suggestive of a eunuchoid stature. There were no voice changes except in a 65-year-old patient suspected of having leprous laryngitis. Thyroid cartilage was normal in all subjects examined.

It is difficult to evaluate the shaving habits accurately in this group of patients. Many were Negroes from the Virgin Islands, who characteristically had a scanty beard.

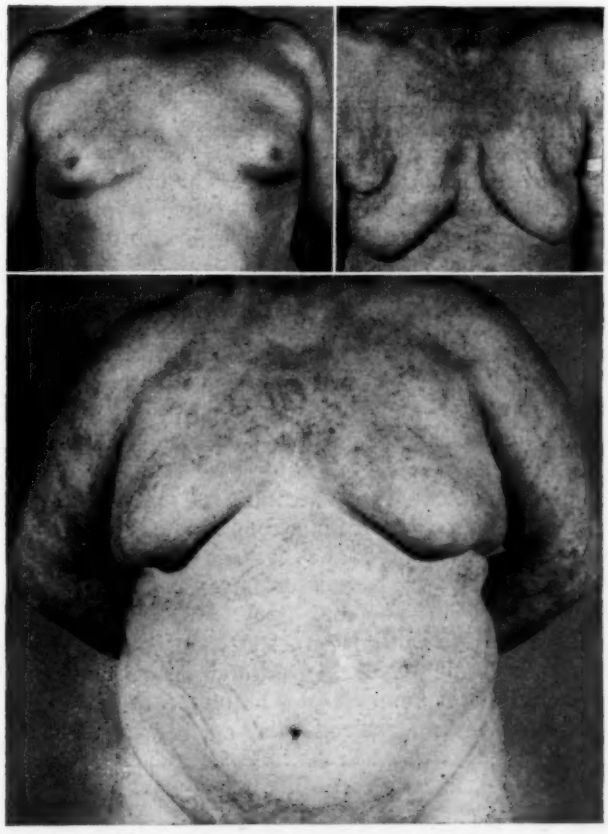

Fig. 5.—Types and degrees of gynecomastia.

Many nonleprous patients reportedly shaved only once or twice weekly. There was no history of impotence in the group, and ejaculations in all were apparently normal. Sperm cell counts were not made. There was scanty trunk distribution of hair in 8 of 25 patients and sparse axillary hair in 5 of 25. It must be remembered, however, that leprosy in itself produces changes associated with decrease in body hair. In general, then, these patients have not had classical eunuchoid characteristics.

A history of orchitis was obtained in 9 of 25 patients with atrophy, an incidence of 36%. This figure is rather high, and it is suggested that in many epididymitis, and not true orchitis, is the significant lesion. The sizes of testes varied from 4.7 by 3.0 to 1.7 by 1.4. These testes are not so small as to be immeasurable and are, therefore, slightly larger than those described in the group with the Klinefelter syndrome.[10]

The 17-ketosteroids were normal (7.8 and 9.7 mg. per 24 hours), and gonadotropins were markedly elevated (less than 288 and more than 384) in two subjects, only one of whom had gynecomastia. In the method utilized in these determinations no attempt is made to separate follicle-stimulating hormone and luteinizing hormone, and they are reported at total gonadotropins.

COMMENT

It is important to differentiate the terms "testis atrophy" and "hypogonadism" or "hypogenitalism." Whereas not all subjects with atrophic testes show overt manifestations of clinical hypogonadism, the vast majority with hypogonadism have either atrophic or completely absent testes (true eunuchism).

Rolnick [11] uses the term "primary hypogenitalism" to denote deficiency of pituitary gonadotropic factor with secondary testis failure. The more accepted terminology reserves the term "primary hypogonadism" for conditions involving intrinsic testis defects of either seminiferous or of interstitial cell elements. Secondary hypogonadism then implies the failure of either the production or the release of gonadotropic hormones. The classical causes of testis atrophy are legion and include cryptorchism; direct trauma; surgical trauma, as following orchiopexy or other scrotal surgery; vascular lesions, including infarction or torsion; senility; mumps; prolonged hyperpyrexia; debility; irradiation; avitaminosis; cirrhosis; schizophrenia; hypothyroidism; diethylstilbestrol therapy; diseases of the pituitary and hypothalmus; pseudohermaphroditism and true hermaphroditism; and inflammatory lesions, including leprosy. The atrophic testis is as vulnerable to secondary disease processes as is the normal testis. Seminoma and interstitial cell tumor formation have both been described in atrophic testes.[12] Secondary disease processes in the testes of those with clinical hypogonadism, however, have interestingly enough not been described.

In 1942 Klinefelter, Reifenstein, and Albright [10] reported in some detail a syndrome characterized by hyalinization of seminiferous tubules in small testes, aspermatogenesis, gynecomastia, normal Leydig cells, normal or decreased 17-ketosteroids, and increased follicle-stimulating hormone. These findings were described in nine subjects. Heller and Nelson [13] in 1945 described a similar entity. These authors studied 20 patients within a period of one year and had 30 additional cases over this same period that were not reported. They stressed the frequency of this syndrome. Three constant features of the syndrome were described by Heller and Nelson as (1) small testes, (2) azoospermia, and (3) high level of gonadotropins. Nine variable features were referable to skeletal changes, gynecomastia, external genitalia, hair distribution, pitch of voice, muscular development, Leydig cell appearance, 17-ketosteroid excretion, and excretion of estrogens. After a comparison of these features with those observed in the subjects described herein, it is apparent that we are dealing with what seems to be a very similar disease process. We have observed atrophic hyalinized testes, normal levels of 17-ketosteroids, elevated levels of gonadotropins, and gynecomastia, the more constant features. Perhaps leprosy is one of the known causes of this syndrome characterized by hypergonadotropic eunuchoidism.

An often neglected, yet important, phase of studies of testicular atrophy is associated liver disease. In 1926 Corda [14] reported a case of hepatic cirrhosis with associated testicular atrophy and gynecomastia. Since that time many similar reports have been described. Bennett, Baggenstoss, and Butt [15] have recently reported the study of another group of cirrhotic patients with testicular atrophy and gynecomastia. It has been suggested that in patients with severe liver disease, including cirrhosis, the normal inactivation of estrogen is interfered with and increased amounts are responsible then for such changes as gynecomastia. There appears to be no consistent correlation between liver damage and testicular atrophy in our series, in that cirrhosis has not been observed at any of the autopsies.

That any of these syndromes may exist without all the factors that go into its composition does not seem unreasonable. As Heller and Nelson remark in their study, "Because they lack gynecomastia these cases cannot be regarded as examples of the syndrome as originally described (by Klinefelter et al.); yet we hesitate to call these cases examples of a new and separate syndrome." The same might be applicable to these patients with leprosy. We agree with Heller and Nelson and believe that these may be a part of a rather large group of hypergonadotropic eunuchoids, and we hesitate to create a new name for the condition in these cases.

It is known that the testis produces two definite hormones: testosterone and estrogen. It is not within the scope of this paper to discuss the matter of a third hormone of the testis. Briefly it has been postulated that the Sertoli cells of the seminiferous tubules or the germinal epithelium itself produces an "x-hormone," called variously "inhibin" or "contruin," which is a pituitary antagonist. The functions of this second hormone include the inhibition of production of follicle-stimulating hormone, the support of spermatogenesis, and inhibition of the mammotropic hormone. With an absence of this hormone as would of necessity occur with hyalinization of the seminiferous tubules, there is then an increase in

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production of follicle-stimulating hormone, azoospermia, and gynecomastia. It should be noted that there are several good theories that militate against the presence of a third hormone. One such theory (Heller and Nelson) is that the elevated gonadotropins result from failure of the seminiferous tubules to utilize follicle-stimulating hormone.

No specific therapy has been undertaken for the testicular atrophy or gynecomastia per se. Since this group of patients possibly fits into the group of hypergonadotropic eunuchoids, it is not likely that pituitary hormone in any form would be of avail. Heller and Nelson have reported favorable response in their group to substitution androgen therapy. This may be of some value in patients with leprosy, but it has not been tried to date.

SUMMARY AND CONCLUSIONS

Genitourinary tract involvement in patients with leprosy is briefly described. One hundred seventy-nine male patients with leprosy (Hansen's disease) were examined with respect to atrophy of the testes and gynecomastia. Twenty-eight per cent were found to have atrophy, and 19% were found to have gynecomastia. In addition, a histological study of the testes of 20 subjects with leprosy is reported. This includes material from autopsy and surgical biopsy. A rather characteristic picture of leprous orchitis with infiltration of the vessel walls and adjacent tissues by Mycobacterium leprae, interstitial cell clumping, and atrophy of seminiferous tubules progressing to complete fibrosis and obliterating endarteritis is described. The 17-ketosteroids were normal and gonadotropins were increased in two of the subjects whose testes were subjected to biopsy.

It is suggested that this group of patients, despite their not presenting typical eunuchoid features, fits into the general category of hypergonadotropic eunuchoids described by Klinefelter, Reifenstein, and Albright and by Heller and Nelson, with characteristic atrophic testes, normal 17-ketosteroids, elevated level of gonadotropins, and gynecomastia. It is postulated that leprosy is perhaps one of the few disease entities of this group in which the etiological factors are known.

LEFT RECURRENT LARYNGEAL NERVE PARALYSIS IN ARTERIOSCLEROTIC HEART DISEASE

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and
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Hoarseness due to left recurrent laryngeal nerve paralysis is a rare occurrence in patients with congestive heart failure of any cause but is most commonly seen with severe mitral stenosis, and less commonly with congenital heart disease,[1] when marked dynamic dilatation of the left pulmonary artery compresses the nerve against the aortic arch, its adjacent lymph nodes, and the ligamentum arteriosum.[2] It is extremely uncommon in patients with arteriosclerotic heart disease, having been reported previously only by King, Hitzig, and Fishberg.[3]

REPORT OF A CASE

A 55-year-old white male married engineer was first admitted to Winter Veterans Administration Hospital Aug. 12, 1948, complaining of short attacks of substernal pressure-like pain, occasionally radiating down both arms, during the previous two winters. He had also noticed easy fatigability and shortness of breath on exertion since February, 1948. This became severe and accompanied by nocturnal dyspnea in June, 1948. Since that he had been treated with digitalis, with improvement. For the two years prior to examination his voice would break occasionally for a few seconds at a time. On June 1, 1948, he awoke in the morning with hoarseness, which remained until the time of admission.

At the time of physical examination the patient was in no distress. His blood pressure was 110/90. His pulse was regular, with a rate of 72. The heart tones were somewhat faint, and there were no murmurs. The lung fields were clear to auscultation and percussion. The peripheral vessels were not remarkable. There was no cyanosis, edema, or clubbing. Laryngeal examination revealed complete paralysis of the left vocal cord. The arm to tongue circulation time (tested with dehydrocholic acid) was 27 seconds. The chest roentgenogram revealed enlargement of the left ventricle. Fluoroscopic examination of the mediastinum revealed no apparent cause for pressure on the left recurrent laryngeal nerve. The patient was fully digitalized, with prompt relief of dyspnea.

After discharge from the hospital on Aug. 30, he continued to take digitoxin for seven months, without shortness of breath. His hoarseness began to diminish at the time of discharge and completely disappeared five weeks later. Seven months after he left the hospital he stopped taking digitoxin on the advice of his family physician. Six weeks prior to his second admission, on July 29, 1951, he began to notice gradually progressive weakness, orthopnea, and nocturnal dyspnea and his hoarseness returned. He consulted a laryngologist, who found "inflammatory laryngitis" and referred him to an internist, who advised hospitalization.

Physical examination on the second admission revealed the patient to be dyspneic and in obvious respiratory distress. There was no distention of the neck veins. There were moist rales at both lung bases, with some dulness and diminished breath sounds at the base of the right lung. The blood pressure was 130/90. The pulse was regular, with a rate of 96. The heart sounds were distant, and no murmurs were heard. The liver edge was palpable 2 cm. below the costal margin and was not tender. There was no ankle edema. Laryngeal examination revealed complete paralysis of the left vocal cord.

Results of routine hematologic studies, including the sedimentation rate, were normal. Urinalysis and serologic studies disclosed no abnormalities. The serum cholesterol was 341 mg. per 100 cc. The plasma chlorides were 95 mEq. per liter, and carbon dioxide was 45 vol. %. The basal metabolic rate was +1%. A chest roentgenogram revealed obliteration of the right costophrenic angle, with a uniform density over the lower third

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From the Medical Service, Winter Veterans Administration Hospital.

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3. King, F. H.; Hitzig, W. M., and Fishberg, A. M.: Recurrent Laryngeal Paralysis in Left Ventricular Failure, Am. J. M. Sc. **188**: 691-697, 1934.

of the right lung. The heart appeared enlarged to the left, and there was some widening of the aortic arch. A chest roentgenogram on Aug. 10 revealed clearing of the right lung base. Electrocardiograms revealed left bundle branch block. The arm to tongue circulation time (tested with dehydrocholic acid) was 30 seconds; ether circulation time was 9 seconds. The vital capacity was 4.6 liters (99% or normal).

Fluoroscopic examination revealed moderate elongation of the left ventricular inflow and outflow tracts, with some hilar congestion and moderate posterior bowing of the esophagus by enlargement of the left auricle. An unusually low aortic arch was seen in the left anterior oblique view to encroach on the aortic window close to the left pulmonary artery.

Digitoxin was again given to toxicity levels, because of the slow decrease in circulation time and the persistent pulmonary basal rales. Weakness, orthopnea, and nocturnal dyspnea improved within a few days after digitoxin therapy was started. However, dyspnea on exertion persisted. At the time of discharge on Oct. 27, his hoarseness had begun to improve.

Sudden death, presumably a result of coronary occlusion, occurred Jan. 2, 1952. No autopsy was performed.

COMMENT

The primary cardiac strain in patients with arteriosclerotic heart disease is nearly always on the left ventricle, in contrast to the primarily left auricular strain imposed by mitral stenosis. Only when the arteriosclerotic left ventricle fails does increased pressure occur in the left auricle and pulmonary vessels. The right ventricle does not, as in patients with mitral stenosis, enjoy a prolonged period of adjustment to the increased strain. When failure of the left ventricle occurs, it is apt to be of relatively rapid onset, or intermittent in character, as in paroxysmal nocturnal dyspnea or exertional dyspnea, with sudden imposition of strain on the right ventricle.

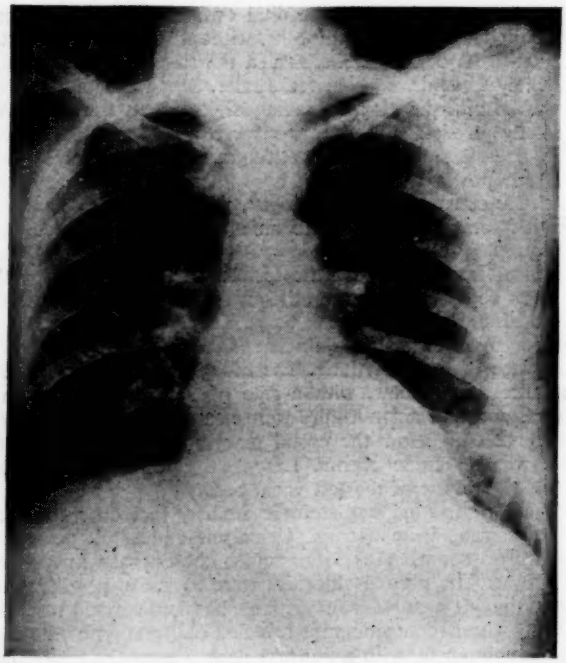

Fig. 1.—Posteroanterior view of the chest, 6-ft. focal-film distance. Note the low position of the aortic knob, elongation of the left ventricular outflow tract, and pulmonary congestion.

The extreme degree of chronic pulmonary congestion often seen with mitral stenosis is rare in patients with arteriosclerotic heart disease. The right ventricle fails more rapidly in the latter, with consequent relief of pulmonary hypertension. If dynamic dilatation of the left pulmonary artery is the common basis of recurrent laryngeal nerve compression, one would not, therefore, expect its occurrence other than rarely in patients with arteriosclerotic heart disease.

In our patient, left ventricular failure had been continuous, though varying in degree, for nearly four years. At no time had right heart failure appeared. In this respect he resembles patients with mitral stenosis, in having had prolonged pulmonary congestion and right heart strain. This is evident not alone in his symptomatic history and physical examination findings, but also in his circulation times, which had persistently shown relatively normal right heart (arm to lung) times with markedly prolonged left heart (lung to tongue) times. Digitalization even to toxicity, low-salt intake, and treatment with mercurial diuretics had not relieved entirely his left heart failure; insofar as relief was achieved, the hoarseness and vocal cord paralysis cleared repeatedly.

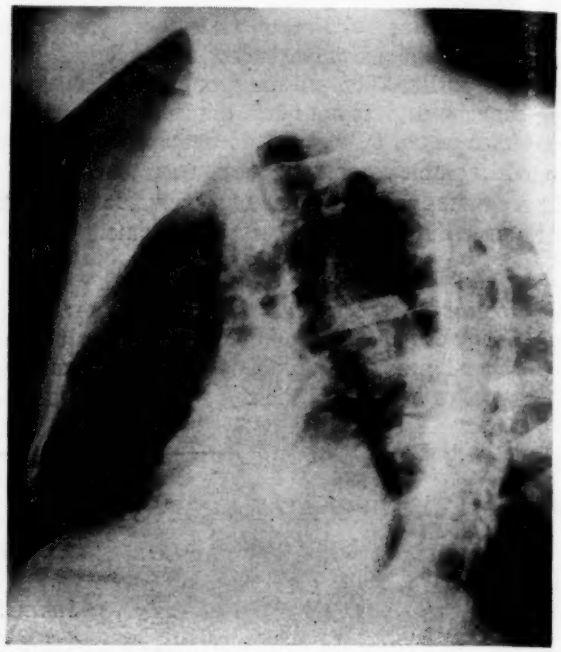

Fig. 2.—Left anterior oblique view of the chest, 6-ft. focal-film distance. Note the low position of the aortic arch, almost completely obliterating the usual "aortic window" between it and the pulmonary artery. The inflow tract of the left ventricle is elongated and fails to clear the spine.

An additional factor in the recurrent laryngeal nerve compression in this case may well have been the unusually low position of the aortic arch in relation to the left pulmonary artery. This was evident in the low position of the aortic knob seen on the roentgenogram (fig. 1) and was confirmed on fluoroscopic examination. The low position of the transverse portion of the aortic arch was seen to reduce sharply the vertical diameter of the "aortic window" in the left anterior oblique view, very nearly obliterating it (fig. 2). Very little pulmonary artery dilatation would, in this circumstance, suffice to compress the recurrent nerve against the aorta.

SUMMARY

The rare occurrence of left recurrent laryngeal nerve paralysis with arteriosclerotic heart disease is reported and its pathogenesis discussed. It is suggested that an unusually low transverse aorta encroaching on the "aortic window" was partially responsible for the nerve compression in the case reported.

APLASTIC ANEMIA ASSOCIATED WITH ADMINISTRATION OF CHLORAMPHENICOL

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and
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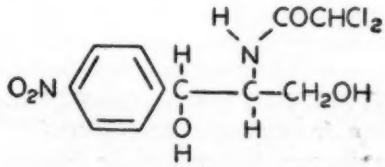
One of the most frustrating of the problems that confront the hematologist always has been aplastic anemia. He thinks that somewhere in the patient's environment may be an agent responsible for the suppression or failure of the bone marrow and that, if the agent could but be found and removed, recovery might result. Seldom is such an agent found although occasionally some new commercial solvent, some new commercial process using old solvents, or some new drugs introduced into the therapeutic field prove to have toxic effect. Individual idiosyncrasy for many of these agents, however, complicates the problem tremendously.

General experience in the past has shown that even though newly introduced drugs are stated, on the basis of careful experimental and clinical study, to have no injurious effect on hematopoietic tissues, long and extensive clinical administration may be required before possible sensitivity reactions are demonstrated. This is probably best shown by the history of amidopyrine, which was discovered chemically in 1889 but was not introduced into medicine until some years later. Amidopyrine was used extensively during the years shortly before and after 1920, and it was not until 1934 that Madison and Squier [1] published their data showing that some persons had specific sensitivity to this drug that resulted in the development of acute granulocytopenia. Although the time between the introduction of other drugs and the discovery of untoward reactions has been shorter in many instances, it is now recognized that a great many drugs may have profound effect on the bone marrow and that this effect may be irreversible and fatal. To cite only a few such instances: (2-isopropyl-4-pentenoyl) urea (sedormid®) may specifically affect the circulating platelets; sulfonamide drugs have been reported to produce a variety of blood dyscrasias; and the same is true of the goitrogenic preparations, such as 2-thiouracil and propylthiouracil. The fact that these useful drugs have such effect does not invalidate their use. However, the attending physician must be aware of possible toxic effects and must take appropriate steps for their recognition. Recently reports have appeared that indicate that use of chloramphenicol may be associated with aplastic anemia.

Crooks [2] stated that chloramphenicol (chloromycetin®), which is the active material obtained from an actinomycete selected from a sample of Venezuelan soil by Burkholder, is chemically a para-nitrophenylpropane derivative. It is named D-(-)-threo-2-dichloroacetamido-1-*p*-nitrophenyl-1, 3-propanediol. The formula is shown in the figure.

This material was the first of the naturally occurring antibiotics to be synthesized chemically, and the synthetic material is identical physically, chemically, and biologically with the drug produced by fermentation. Although investigators were aware that nitro groups never have been found in nature or associated with living processes except in a toxic manner, pharmacologic studies failed to show the expected toxicity except that, in experimental studies on dogs, transitory anemia appeared.[3]

Volini and associates,[4] in the spring of 1950, reported on their experience with three patients who were receiving chloramphenicol in therapeutic doses. Severe, reversible granulocytopenia and hypoplasia of bone marrow developed, with both an erythroid and granulocytic arrest of maturation. One of their patients had severe anemia in the course of uncomplicated typhoid four days after discontinuance of the treatment. The investigators commented, "The toxic manifestations of this drug in man will have to be studied more extensively before it can be considered an absolutely safe therapeutic agent." Later, in 1950, Rich, Ritterhoff, and Hoffmann [5]



Formula for chloramphenicol.

reported a fatal case of aplastic anemia following use of chloramphenicol for infection of the urinary tract of a 63-year-old man. Hematopoietic elements in the bone marrow of this patient were markedly reduced. Gill [6] has reported on granulocytopenia following use of chloramphenicol, but his cases were unusual in that both his patients were young children and that the leukocyte count was within the limits of normal. In one of these cases there was an increase in the percentage of lymphocytes and in the other marked reduction in the percentage of neutrophils: the reduction in the second case was much less marked than in the first. Janbon and Bertrand [7] reported the development of moderately severe anemia

From the Division of Medicine (Dr. Hargraves and Dr. Heck) and Section of Pediatrics (Dr. Mills), Mayo Clinic.

1. Madison, F. W., and Squier, T. L.: The Etiology of Primary Granulocytopenia (Agranulocytic Angina), J. A. M. A. **102**: 755-759 (March 10) 1934.

2. Crooks, H. M., Jr.: Chemistry of Chloromycetin,® Bull. New York Acad. Med. **25**: 792-794 (Dec.) 1949.

3. Smith, R. M., and others: Chloromycetin®: Biological Studies, J. Bact. **55**: 425-448 (March) 1948.

4. Volini, I. F., and others: Hemopoietic Changes During Administration of Chloramphenicol (Chloromycetin®), J. A. M. A. **142**: 1333-1335 (April 29) 1950.

5. Rich, M. L.; Ritterhoff, R. J., and Hoffmann, R. J.: A Fatal Case of Aplastic Anemia Following Chloramphenicol (Chloromycetin®) Therapy, Ann. Int. Med. **33**: 1459-1467 (Dec.) 1950.

6. Gill, P. F.: Agranulocytopenia Following "Chloromycetin": Report on Two Cases, M. J. Australia **1**: 768-769 (June 10) 1950.

7. Janbon, M., and Bertrand, L.: L'anémie du chloramphénicol, Bull. et mém. Soc. méd. hôp. Paris, 1951, pp. 990-996.

without evidences of increased hemolysis or myelotoxicosis in six cases. In four of these the original illness was brucellosis, in one typhoid, and in one tuberculosis. They commented that the anemia was not accompanied by any disturbance of the leukocytes or thrombocytes. Di Lollo [8] has written on "acute hemopathy in the course of chloramphenicol therapy," but we have not as yet been able to obtain his article for review. Loyd [9] more recently has reported a case in which aplastic anemia was due to chloramphenicol. Examination of the bone marrow at necropsy disclosed extensive fat replacement and essentially no evidence of young forms of the granulocytic series; even the megakaryocytes were conspicuous by their absence. In May, Wilson and his associates [10] reported two cases in which aplastic anemia followed prolonged administration of chloramphenicol.

In 11 months we have had eight referred cases of aplastic anemia in which we have been able to establish a history of ingestion of chloramphenicol. The relationship of the medication to subsequent events, both in time and in sequence, leads us to believe that this relationship is one of cause and effect. A ninth case is included in this series, although the patient was not ours; she served as a control patient for one of the eight who have been mentioned. The attending physician gave us the data, and he was the home physician of our parallel case. A 10th case is included since we saw the patient in 1950. Only in retrospect, however, did we realize that her aplastic anemia was intimately associated with daily ingestion of small doses of chloramphenicol, and she has evidently completely recovered since the drug was withdrawn. Seven of the other nine cases have terminated fatally, and two patients are currently under observation.

Since in all cases the hematologic difficulty was established by the time the patients reached Rochester, many fellow physicians and technicians throughout the country supplied us with invaluable data. These data consist of past and follow-up medical histories and antecedent and follow-up laboratory findings, as well as reports of necropsy when available. The report could not have been made without the cooperation of the physicians and families in documentation of medication and notation of the temporal relationship of the medication to the symptomatology of the aplastic anemia.

REPORT OF CASES

Case 1.—A white girl, 11 years of age, was admitted on March 7, 1952, with the complaint of hemorrhage. Except for mild hay fever on occasion, as well as repeated infections of the upper respiratory tract, she had been relatively well previously. Appendectomy had been performed in 1947 for recurring lower abdominal pain, and other characteristics of appendicitis, and, except for mild hypochromasia, results of studies of the blood had not been remarkable at that time.

In February, 1951, tonsillectomy and adenoidectomy had been performed. Considerable hemorrhage from the site of adenoidectomy had required two transfusions of blood, of 500 cc. each, for replacement. Laboratory data before the operation had been satisfactory. The hemoglobin value was 77%. There were 3,750,000 erythrocytes per cubic millimeter of blood, and 6,000 leukocytes, with 46% lymphocytes, 51% neutrophils, and 3% eosinophils. The bleeding time was one minute, and the coagulation time four minutes.

In June, 1951, when the patient and her mother had been visiting in a city near their home, both had had an acute febrile illness. The patient was taken into a hospital, largely because of a "polio scare" and, according to her mother, "blood counts, urinalysis, and physical examination were normal."

The patient then had been well until Christmas, 1951, when another acute febrile illness had occurred, and in the absence of her own physician another one had been called. According to the mother, the girl had been given a "bottle of chloromycetin® liquid which she took in doses every few hours until the bottle was empty." After this she "took a couple of capsules of chloromycetin®" to complete treatment. Reaction to the drug had not been noted, and the patient had recovered without evident sequelae.

In the last week of January, 1952, or one month after the patient had taken chloramphenicol, as has been related, she had had another infection of the upper respiratory tract and chloramphenicol again had been prescribed at the rate of "1 capsule every four hours for 4 capsules and then every six hours until 12 were taken." The mother stated that the child "got sick and vomited" before the course of treatment had been completed, and the mother had stopped giving her the capsules.

On Feb. 27 petechiae first had been noted by the patient, and on March 2 she had been taken to her physician. Except for the purpura and a positive tourniquet test, results of physical examination had not been remarkable. Laboratory work at this time had revealed a hemoglobin value of 9.5 gm. per 100 cc., and 3,390,000 erythrocytes per cubic millimeter. There were 4,150 leukocytes, with 97% lymphocytes, and 3% neutrophils. There were 80,000 thrombocytes and no reticulocytes. The bleeding time was more than 30 minutes. The clot retraction was "20% in nine hours," and the coagulation time 13 minutes. Sternal aspiration "showed a marked hypoplasia of all blood cell types."

On March 7, as has been said, the girl was admitted to the Mayo Clinic and the foregoing history was obtained. Results of physical examination were not remarkable other than that there were petechiae and ecchymotic areas in the skin and mucous membranes. Laboratory work gave the following results: Urinalysis revealed grade 1 red blood cells. The hemoglobin value was 9.1 gm. per 100 cc., and there were 3,180,000 erythrocytes, and 3,900 leukocytes. A differential leukocyte count revealed 95% lymphocytes, 1% monocytes, 2% neutrophils, 1 % eosinophils, and 1% basophils. There were 20,000 thrombocytes and no reticulocytes.

In the blood smear immature or abnormal forms were not seen. There was only a rare granulocyte, and the blood thrombocytes were greatly reduced in number. The erythrocytes gave no evidence of regeneration. Volumetric study of aspirated bone marrow revealed a myeloid-erythroid (nucleated cell) layer of only 2% (normal 4 to 8%). In smears of the bone marrow only a rare granulocyte or normoblast was seen and only one megakaryocyte could be found. The rest of the cellular elements were small lymphocytes and plasmacytes, with an occasional reticuloendothelial cell. Fixed tissue of the marrow showed it to be composed mostly of fatty tissue, with a few collections of lymphocytes and plasmacytes.

The patient was returned to her home physician for supportive care but soon "fulminating purpura" developed, with gingival bleeding and massive pulmonary hemorrhages. She died April 8, 1952, one month after we had first seen her.

Case 2.—A man, 42 years of age, was admitted on June 19, 1951. In 1942, he had had septic sore throat, which had been treated effectively with sulfadiazine. In 1947 a duodenal ulcer had required nonsurgical treatment for three months. There was also a history of past sensitivity to penicillin (urticaria).

On April 12 and 13, 1951, a furuncle had developed on the chin. It had drained persistently and had not responded to symptomatic treatment. Because of the known sensitivity to penicillin, capsules of chloramphenicol had been given as follows: 1 capsule every four hours for 6 doses; 1 capsule every six hours

8. Di Lollo, F.: Acute Hemopathy in the Course of Chloramphenicol Therapy, Acta med. Patavina 12: 395-417, 1951.

9. Loyd, E. L.: Aplastic Anemia Due to Chloramphenicol, Antibiotics and Chemother. 2: 1-4 (Jan.) 1952.

10. Wilson, L. E., and others: Aplastic Anemia Following Prolonged Administration of Chloramphenicol, J. A. M. A. 149: 231-234 (May 17) 1952.

for two more days. A total of 14 capsules had been given. About a week later, (April 19 or 20) the man again had taken 1 capsule every four hours for 4 doses.

On April 22, jaundice had been noted and four days later the patient had been admitted to his local hospital. In the history taken at that time it was recorded that he had "become ill a week ago after eating a ham salad sandwich, and had nausea, vomiting and vertigo." (This was the time of his second course of chloramphenicol.) Following the episode related in the quotation, the nausea and anorexia had persisted, along with the developing jaundice.

Results of laboratory work done at his local hospital were reported as follows:

The hemoglobin value was 99.5%. There were 5,190,000 erythrocytes and 5,850 leukocytes. A differential leukocyte count revealed 45% lymphocytes, and 54% neutrophils. The icterus index was 29.2. A van den Bergh test revealed 3.8 mg. of bilirubin per 100 cc. by direct reaction. The prothrombin level was 79%. The sedimentation rate was 12 mm. per hour (Westergren). Tests of stools for occult blood were negative. Serologic tests for syphilis were negative. Gastrointestinal roentgenograms revealed no gross abnormalities, and the comment was "liver and spleen shadows appear within normal limits."

In his referring letter the attending physician commented: "Our impression was that he had a toxic hepatitis." The patient stated "the jaundice cleared 100% in three days" and said that he had felt well thereafter.

The man came to the Mayo Clinic for examination and was admitted on the date given at the start of the report of this case, about two weeks after his dismissal from his local hospital. The only abnormalities found on physical examination were a few petechiae where his shoulders had rubbed on the back of the seat of the automobile while traveling, petechiae about the waist, where his belt had rubbed, and other petechiae on the legs and ankles. The patient had not noticed the petechial spots. Laboratory work at this time gave the following results:

Urinalysis revealed red blood cells, grade 2. The hemoglobin level was 13.4 gm. per 100 cc., and there were 4,400,000 erythrocytes and 5,800 leukocytes. The differential leukocyte count revealed 49.5% lymphocytes, 2% monocytes, 47.5% neutrophils, and 1% basophils. There were 18,000 thrombocytes. The report on the blood smear was "Marked thrombocytopenia; some increase in lymphocytes; no immature forms were seen." There was no serum bilirubin on the direct test, with a level of 1.2 mg. per 100 cc. revealed by the indirect test. The flocculation test for syphilis was negative. The prothrombin time was 19 seconds. In a liver function test with sulfobromophthalein (bromsulphalein®) there was no dye retention in one hour.

A chest roentgenogram revealed no abnormalities. A gallbladder roentgenogram showed a normally functioning gallbladder. Volumetric study of aspirated bone marrow material revealed only a 1% nucleated cell layer. The report of smears of bone marrow read, "All elements are reduced. Megakaryocytes are virtually absent. The majority of the cellular elements are lymphocytes and plasmacytes." The description of fixed sections of the bone marrow stated that there were "small units which show the structure of a hypocellular marrow. Lymphocytes are the predominant cell."

In our opinion aplastic marrow was developing in this case, and the patient was dismissed with the advice to be under constant observation at home and to receive transfusions as he might need them. During the period June 25 to 30 inclusive, laboratory findings at the patient's home were essentially the same as those just noted. In this same period he received transfusions of 3 pints (approximately 1,500 cc.) of blood.

On July 1, the man was seen at another medical center and the physicians there supplied the following data: There were 2,400,000 erythrocytes, and 4,000 leukocytes. On a differential leukocyte count there were 55% lymphocytes, 5% monocytes, and 40% neutrophils. On blood smears the cells were qualitatively normal in appearance. Sternal aspiration revealed "markedly acellular bone marrow with only a rare normoblast and no megakaryocytes seen." There was, however, a "fair representation of myeloid cells." In view of these findings, it was suggested that cortisone might be used in addition to treatment by transfusion.

Following the patient's return home, bleeding continued, and he was admitted in emergency condition to another hospital on July 28. His attending physician and the staff pathologist have reported the findings of his final hospitalization. Physical examination disclosed the presence of multiple petechiae and ecchymotic lesions of the skin, as well as multiple areas of bleeding and ulceration in the mouth, including the gums. There was tenderness of the left lower extremity. (This raises the question whether there was hemorrhage into the muscles.)

Results of laboratory work done on July 28 were reported as follows:

The hemoglobin level was 9.2 gm. per 100 cc. There were 2,850,000 erythrocytes, and 2,400 leukocytes, with 96% lymphocytes, 2% monocytes, and 2% neutrophils. There were 19,000 thrombocytes. The coagulation time was seven minutes and four seconds, and the bleeding time was two and one-half minutes (?). The prothrombin time was 68% of normal.

The patient had moderate elevation of temperature while in the hospital. Terminally Cheyne-Stokes respiration developed, and the man died four days after his admission. Significant findings at necropsy included considerable blood in the subarachnoid space, as well as evidence of hemorrhage in other organs. The liver, spleen and lymph nodes appeared grossly normal. Microscopically, the structure of the liver and the spleen seemed undisturbed. Concerning the bone marrow, the report was, in part, as follows: "Its cellularity varies considerably in different areas. In some, the marrow is found to be quite cellular while, in others, it is largely fatty. We fail to see megakaryocytes. Erythroid and myeloid elements also seem to be diminishing."

—CASE 3.—This white girl, 3 years of age, was admitted on March 19, 1951, because of severe bleeding. She had had repeated infections of the upper respiratory tract but otherwise her past history and family history were not remarkable. Three siblings were living and well.

About five weeks before admission she had had acute pharyngitis and had been treated with "about 20 capsules of chloromycetin® during the three weeks" before the onset of her hemorrhagic tendency. Two weeks before admission, petechiae and ecchymotic areas had developed on the body. "Some penicillin and vitamin K" were given at this time. Severe and persistent epistaxis had appeared and repeated transfusions of blood, totaling 1,250 cc. had been administered. Studies of blood and bone marrow had indicated that the girl had hypoplastic anemia.

At the time of admission to the Mayo Clinic, the patient was acutely ill; her temperature was 103 F. Physical examination revealed multiple petechiae and ecchymotic areas and the girl was actively bleeding around the nasopharyngeal pack, which was in place at the time of her admission. Adenopathy or other abnormalities were not noted.

Laboratory studies made while she was in hospital in Rochester revealed the following:

The results of urinalysis were normal. The hemoglobin level decreased from 15.5 to 9.2 gm. per 100 cc. The erythrocytes decreased from 5,030,000 to 2,710,000, and the leukocytes from 1,700 to 600, with lymphocytes increasing from 95 to 97%, monocytes from 1 to 3%, and the neutrophils from 1 to 2%. The thrombocytes varied from 5,000 to 22,000. There were 0.1% reticulocytes. Blood smear revealed marked neutropenia and thrombocytopenia. The blood urea level was 32 mg. per 100 cc. The prothrombin time was 21 seconds. A chest roentgenogram revealed no abnormality. Volumetric study of aspirated bone marrow material revealed a myeloid-erythroid layer of only 1%.

The patient was in the hospital for nine days. The course of the illness was stormy, and her temperature ranged from 99 to 104 F. Treatment consisted of four blood transfusions of 250 cc. each. By mouth, each day, the patient received 750 mg. of aureomycin, as well as 100 mg. of cortisone. She died on March 27, from massive gastrointestinal hemorrhage.

Necropsy revealed markedly hypoplastic bone marrow, with little evidence of hematopoiesis. There was a relative increase in reticuloendothelial cells and lymphocytes. Hemorrhages were numerous and diffuse in many viscera, and moniliasis of the esophagus, stomach, spleen and kidneys was observed.

CASE 4.—This white girl, 5 years of age, was admitted on Dec. 6, 1951, with a chief complaint that purpura had been present for four weeks. A subordinate complaint was of chicken pox of four days' duration. The girl had had the usual infections of childhood. Her past history and her family history were not remarkable.

Four weeks before admission, bruises, which were unusual for her, had appeared. About a week later noticeable irritability had developed, and she had begun to have spontaneous epistaxis. By the time another week had passed, definite petechiae had appeared. Rutin and vitamin K had been given at this time. During this period, the patient's 8-year-old brother had had chicken pox and, on Dec. 2, the patient and her 6-month-old brother both had displayed the first signs of chicken pox. By the evening of Dec. 3, the vesicles of chicken pox had appeared on the girl's body and had become hemorrhagic. Meanwhile her temperature became elevated. The temperature ranged from 103 to 105 F until the time of admission to the hospital in Rochester. On Dec. 3, she had received aureomycin, 150 mg. every four hours, and 300,000 units of penicillin twice a day. On Dec. 4, she had vomited blood-streaked material and administration of aureomycin had been discontinued. The daily dose of penicillin had been increased to 1,000,000 units on Dec. 5.

On Dec. 4, the concentration of hemoglobin had been 11.6 gm. per 100 cc. of blood. Erythrocytes had numbered 3,360,000 and leukocytes 1,240 per cubic millimeter of blood.

The patient had received 18 capsules of chloramphenicol of 50 mg. each in late August, 1951. In October of the same year, also, she had been given *p*-benzylphenyl carbamate ("diphenan"), 0.25 gm. three times a day for seven days, for pinworms.

On physical examination in Rochester, the child appeared to be alert but acutely ill. A severe, hemorrhagic, vesicular rash extended "from head to toe." The lesions varied from ordinary maculae to hemorrhagic vesicles, 3 mm. in diameter, with numerous associated petechiae and ecchymotic areas. The gums were bleeding, and there were numerous small areas of hemorrhage and ulceration in the mouth and pharynx. Adenopathy worthy of remark and hepatosplenomegaly were not found. The temperature was 103 F and a pulse rate of 110 per minute was charted.

Laboratory findings were as follows: The urinalysis revealed no abnormalities. The hemoglobin level was 8 gm. per 100 cc. There were 3,080,000 erythrocytes, and 3,200 leukocytes, with 91% lymphocytes, 2% monocytes, and 7% neutrophils. There were 41,000 thrombocytes. The bleeding time was 14½ minutes. The sedimentation rate was 72 mm. per hour (Westergren). There were from 0.3 to 1.1% reticulocytes.

The report on the blood smear read, "Left shift and toxic changes in neutrophils seen. Moderate number of plasma cells with a few atypical lymphocytes. Very rare platelet seen. There is no myeloid immaturity found." Bone marrow obtained by sternal aspiration revealed, on volumetric study, no demonstrable myeloid-erythroid layer. In smears of the bone marrow there were an occasional normoblast and myeloid element. No megakaryocytes were seen, but a few platelets were encountered. The predominant cells were adult lymphocytes. Material for study of fixed sections was not obtained. A chest roentgenogram, made with portable apparatus, revealed conditions that were within normal limits.

The course of the illness for the 14 days while the patient was in hospital was satisfactory. Four blood transfusions and daily penicillin therapy were given for support. Meanwhile, the lesions of chicken pox cleared and the temperature fell to normal. The concentration of hemoglobin could not be maintained, however; after it had been raised from 7.2 gm. to 11 gm. per 100 cc. of blood, by means of transfusions, it was back to 8.4 gm. at the time of dismissal. The other blood values, on repeated reexamination, stayed essentially within the same range as those in the initial studies.

In the interval of four weeks while the patient was away from the clinic, she received two blood transfusions, one of 200 cc. and the other of 250 cc. When she returned on Jan. 22, 1952, the only remarkable features discovered on physical examination were many petechiae and ecchymotic areas, especially on the legs.

Laboratory work on this occasion gave the following results:

The hemoglobin level was 9.4 gm. per 100 cc. There were 3,010,000 erythrocytes, and 4,800 leukocytes, with 65.5% lymphocytes, 12.5% monocytes, 21% neutrophils, and 1% eosinophils. There were 1% reticulocytes and 35,000 thrombocytes. The blood smear was said to be "essentially same as before."

On Feb. 19, the patient was again brought back to the clinic. In the interval during which she had been away, three more transfusions had been administered. Results of physical examination were negative except for the evidence of purpura.

Laboratory findings were as follows:

The hemoglobin value was 10.5 gm. per 100 cc. The erythrocyte count was 3,510,000 and the leukocyte count 3,700. A differential leukocyte count showed 87% lymphocytes, 6% monocytes, and 7% neutrophils. There were 0.5% reticulocytes and 27,000 thrombocytes. The report on blood smear stated: "Nothing changed over previous reports." Studies of bone marrow obtained on sternal aspiration gave the same results as on the previous occasion.

The final episode of the illness of this patient began on April 1 and terminated 24 hours later with death from cerebral hemorrhage. Her condition had remained essentially unchanged since we had last seen her; she had been active and had felt well most of the time. At 3 a. m. she awoke with a headache and about one and a half hours later started to vomit blood. Throughout the day hematemesis recurred, and, by evening, further signs of cerebral bleeding were developing. She had repeated convulsions until she died.

CASE 5.—This child was not our patient but was a playmate of the girl in case 4. We feel that a brief report of her case should be included in this series for reasons that will become apparent. The physician in the two cases was the same, and he provided the data in this case as well as those parts of the data in case 4 that were gathered elsewhere than in Rochester. The illnesses of the two little girls ran nearly identical courses.

This patient (case 5) received a total of 42 capsules (50 mg. each) of chloramphenicol. These were administered in doses of 100 mg. every six hours from Oct. 13 through Oct. 19, 1951. A careful review of the case with the parents of the child verified the physician's belief that the parents gave no other medication and that the only drug both children had received was chloramphenicol; in other words, *p*-benzylphenyl carbamate was not a factor in this case (case 5).

Aplastic anemia developed, and the course of the illness was the same as that in case 4. The cause of death was cerebral hemorrhage. To quote from the letter of the physician: "Her drug (chloromycetin®) was started about six weeks after Mary's [11]—her purpura appeared on Dec. 18, about six weeks after Mary's and her death came six weeks after Mary's."

CASE 6.—A white girl, 13 years of age, was admitted to the Mayo Clinic on April 8, 1952, complaining of bleeding. The family history was essentially negative; there were three siblings, living and well. There was a personal history of measles at the age of 9 years; of mumps in June, 1951; of appendectomy in November, 1951, and of chicken pox in March, 1952.

The significant part of the history of her present illness goes back to Jan. 26, 1951, when, in her home community, chloramphenicol had been given to her father and the patient had taken 4 capsules (not at the same time) for the "flu." She had not displayed any signs of reaction.

At the end of February, 1952, 13 months later, the patient again had had the "flu." The capsules of chloramphenicol still had been in the house, unused, and the girl had been given 1 capsule at a time for 4 doses.

On March 1, the patient had undergone dental extraction and a dental penicillin-sulfonamide pack had been used. On March 26, petechiae had developed over the feet and limbs. On April 2, a "sore" had appeared on the lower lip and ecchymosis and petechiae had been generalized. On April 4, protracted epistaxis had occurred, and the girl had been admitted to a hospital where laboratory work had revealed a "leukocyte count of 2,200 and no granulocytes present." A blood transfusion of about 500 cc.

11. Mary is the name representing the patient in Case 4, but is not the real name of the patient.

had been given on each of the three following days (April 5, 6 and 7), and the girl had been brought to Rochester where she was admitted directly to hospital.

The patient was normally developed and nourished but petechiae and ecchymotic areas were extensive. The gums were swollen and slightly hemorrhagic, and there was an ulcerated area, 1 cm. in diameter, on the lower lip. Results of the rest of the physical examination were not remarkable. The spleen was not palpable, and adenopathy was not noted. The girl's temperature was 101 F.

Laboratory findings were as follows:

Urinalysis revealed no abnormalities. The hemoglobin level was 14.6 gm. per 100 cc. There were 4,030,000 erythrocytes and 1,400 leukocytes. Differential leukocyte count revealed 94% lymphocytes, 2% monocytes, 2% neutrophils, and 2% eosinophils. There were 51,000 thrombocytes and 0.1% reticulocytes. The bleeding time was 15½ minutes, and the prothrombin time 17 seconds.

The report of the blood smear read, "Only one granulocyte is seen and no immature forms of any type of cell are found. The platelets are considerably reduced on the preparation." Aspirated bone marrow, on volumetric study, yielded a myeloid-erythroid layer of only 1%, while in all smears of bone marrow small lymphocytes predominated. There were some plasmacytes, reticuloendothelial cells, and a rare myeloid-erythroid element among the lymphocytes. In fixed sections there was only fatty marrow containing an occasional nest of cells.

During the period of hospitalization, the course of the illness was septic and the temperature ranged from 100 to 105 F. Acute otitis media yielded material from which Escherichia coli were cultured. After studies to detect sensitivity had been made, the patient was given 0.5 gm. of dihydrostreptomycin intramuscularly twice a day, in addition to 1,000,000 units of penicillin (duracillin®) daily, to protect her in her agranulocytic state. She also received 18 blood transfusions of 500 cc. each, given as they were indicated for bleeding. Cortisone also was given in increasing doses, to 300 mg. daily (intramuscularly), then the quantity was reduced to a maintenance dose of 100 mg. (50 mg. twice a day). When it became evident that the girl's condition was not improving with the help of cortisone, corticotropin was employed and its use was continued for the last four days of her life.

Throughout the 22 days that the patient was in hospital, leukocytes varied in number from 600 to 1,500 per cubic millimeter of blood, 99 to 100% of which were lymphocytes. Thrombocyte counts continued to be below bleeding levels at all times, ranging from 16,000 to 35,000 per cubic millimeter of blood. The cause of death was hemorrhagic pulmonary edema and gastric hemorrhage.

At necropsy, significant findings were: widespread hemorrhage of the viscera, focal necrosis and organizing bronchopneumonia of the right upper pulmonary lobe and terminal hemorrhagic edema of the lungs. Microscopic examination disclosed severe hypoplasia of the bone marrow, with little or no evidence of hematopoiesis.

– Case 7.—A 36-year-old man was admitted to the Mayo Clinic on Feb. 25, 1952, because of a diagnosis, made elsewhere, of hypoplastic anemia with thrombocytopenic purpura. His own past history was not remarkable. His father had Raynaud's disease and diabetes. A sister had died with leukemia, and he had six siblings living and well.

The history of his present illness dated back to June, 1951, when he had had the "flu." He had received penicillin, which had given him hives. In July of the same year, Raynaud's phenomenon had developed in his hands. He had been hospitalized in October for 14 days with pneumonia and had received aureomycin for 10 days and chloramphenicol for 3 days. "His leukocyte count was 4,500 (per cubic millimeter of blood) but the remaining blood picture was normal"; this is the only hematological information we have concerning that illness.

Left cervicothoracic sympathectomy had been performed on Nov. 6 for the persistent Raynaud's phenomenon. Postoperative pleural effusion had developed, and again he had been given chloramphenicol and aureomycin. On Jan. 10, 1952, right cervicothoracic sympathectomy had been performed, at which time the concentration of hemoglobin had been found to be 9.2 gm. per 100 cc. of blood. He had had considerable trouble with bleeding from the nose, the gums, and the wound. Again he had received postoperative treatment with chloramphenicol and aureomycin.

On Jan. 22, he had been readmitted to the hospital with purpura, that is, he had had petechiae and ecchymosis, epistaxis, and hemorrhages into the muscles of the thigh. A diagnosis of thrombocytopenic purpura had been made. The thrombocyte counts then had been 15,000 and 25,000, while studies of the bone marrow had revealed the presence of hypoplastic anemia. Corticotropin had been administered, without benefit, for about 20 days. He had received numerous blood transfusions.

On Feb. 25, the date that was mentioned at the beginning of the report of this case, the patient entered a hospital in Rochester. Laboratory data at this time were as follows:

Urinalysis revealed no abnormalities. The hemoglobin level was 10.2 gm. per 100 cc. There were 3,350,000 erythrocytes and 2,600 leukocytes. The differential leukocyte count revealed 64% lymphocytes, 5% monocytes, 30% neutrophils, and 1% basophils. There were 0.1% reticulocytes and 50,000 thrombocytes.

A blood smear showed leukopenia with toxic neutrophils and marked thrombocytopenia. The bleeding time was more than 30 minutes. The sedimentation rate was 84 mm. per hour (Westergren). Aspirated bone marrow, on volumetric study, yielded a myeloid-erythroid layer of 2%, while study of smears of bone marrow revealed an occasional toxic granulocytic cell, a few normoblasts, but no megakaryocytes. The patient was dismissed five days after his admission with advice to continue with supportive blood transfusions. By correspondence we learned that he died six weeks after his dismissal.

– Case 8.—This white woman, 70 years of age, was admitted to the Mayo Clinic for the fifth time on April 22, 1952. We first had seen her in 1939, when she was 58 years of age. At that time her chief complaint was symptoms of nervous tension. There also was a history of chronic discoid lupus erythematosus with onset in 1932, when the woman had been 51. The lesions had been confined to the scalp and face and had been well controlled by administration of quinine. In 1939, the woman weighed 175 lb. (79.4 kg.), and she had scars from past activity of her lupus erythematosus. Results of physical examination otherwise were not remarkable. Laboratory examinations at this time revealed values within normal ranges.

The woman came to the clinic for a second examination on April 21, 1944, at the age of 62 years. At this time her most significant complaint was urinary frequency of six months' duration, and she had been told that the urine contained pus, casts, and albumin. There were still evidence of her state of nervous tension. She weighed 166 lb. (75.3 kg.) and had alopecia and a blood pressure of 140 mm. Hg systolic and 82 diastolic. Examination of the eye grounds revealed incipient cataracts, grade 2 sclerosis, and grade 1 narrowing of the retinal arterioles, together with multiple, small retinal hemorrhages.

Results of laboratory studies made at this time were reported as follows:

The urine contained albumin, grade 1 to 2, red blood cells, grade 3 to 4, and pus, grade 1. The hemoglobin level was 11.2 gm. per 100 cc. There were 3,490,000 erythrocytes and 6,800 leukocytes. The flocculation test for syphilis was negative. Roentgenograms of the thorax and of the kidneys, ureter, and bladder revealed no abnormalities. The blood urea level was 72 mg. per 100 cc., and the creatinine level 2.3 gm. The urine culture was negative. Excretory urogram and cystoscopic examination revealed no abnormalities. A final diagnosis was made of chronic glomerulonephritis with renal insufficiency.

Our third experience with the patient was in November, 1944, when she was seen at home by one of our staff members in consultation with her home physician. At this time she was convalescing from bronchopneumonia and gave evidence of renal insufficiency and urinary infection. A prescription was given for sulfathiazole, 0.5 gm., three times a day, and a supportive regimen was advised.

She returned to the clinic on Jan. 3, 1949. In the five year interval her condition had not greatly changed. She did complain

anew, however, of very troublesome epigastric distress and increase in exertional dyspnea associated with some substernal distress. Three weeks before this visit she had been awakened with pain in the jaws and in both arms, for which she had been hospitalized. This distress had been recurring about five minutes after meals. Her blood pressure was 155 mm. Hg systolic and 86 diastolic. She was still obese but, otherwise, nothing remarkable was found on physical examination.

Laboratory work on this occasion disclosed the following:

The urine contained albumin, grade 1 to 3, and pus, grade 1 to 2. The specific gravity was 1.003 to 1.010. The hemoglbin level was 15.9 gm. per 100 cc. The erythrocyte count was 4,700,000 and the leukocyte count 7,700. The blood urea level was 58 to 84 mg. per 100 cc., and there was 7.3 mg. of sulfate per 100 cc. The sedimentation rate was 36 to 43 mm. per hour (Westergren). A roentgenogram of the stomach revealed "esophageal hiatal hernia with the cardiac third of the stomach above the diaphragm."

The patient was in the hospital for 37 days on a reduction regimen and conservative treatment for the diaphragmatic hernia was advised. In March, 1952, she had had increasing distress in the thorax and arms while at home. Her erythrocyte count had been 2,400,000 per cubic millimeter of blood and the value for hemoglobin, 9.2 gm. per 100 cc. of blood. Occult blood had been found in the stools. Treatment for peptic ulcer and repeated transfusions of 250 cc. of blood had been given. Results of laboratory work the next week had been reported as follows: There were 2,080,000 erythrocytes and 2,300 leukocytes. The hemoglobin level was 8.2 gm. per 100 cc. There were 65% lymphocytes. There were 43,000 thrombocytes. The stool contained occult blood. The sedimentation rate was 131 mm. per hour (Westergren). Studies of bone marrow had revealed "a hypoplastic marrow with an increase in plasmacytes."

The patient had received five transfusions, after which her erythrocyte count had been 3,200,000 per cubic millimeter of blood and the value for hemoglobin was 9.1 gm. per 100 cc. of blood. On April 22, 1952, as has been said, the patient returned to the clinic for further study, especially regarding the previously reported findings referable to the bone marrow. The pains in the thorax, jaw and arms were about the same as on previous visits. The patient repeated the nontechnical language in which her condition had been explained to her, saying that she had been told that she had a "weak bladder that did not empty well" (residual urine: 350 cc.) and that for the resultant urinary infection she had been receiving chloramphenicol. This drug had been given off and on for two years and, in the last six weeks, the dosage, while variable, "averaged 2 or 3 capsules a day, four or five days a week."

She was still moderately obese (150 lb. [68 kg.]) was pallid, and possibly was slightly icteric. The remainder of the physical examination was not productive of any evidence worthy of remark. Laboratory examinations revealed the following:

The urine contained albumin, grade 2, and pus, grade 1. The hemoglobin value was 11.3 gm. per 100 cc. There were 3,310,000 erythrocytes and 3,800 leukocytes, with 31% lymphocytes, 2% monocytes, 65% neutrophils, and 3% eosinophils. There were 1.1% reticulocytes and 65,000 thrombocytes. The report of the blood smear read, "Platelets markedly reduced, moderate leukopenia, anisocytosis without much polychromasia." The total protein level of the blood was 7.47 mg. per 100 cc. The albumin-globulin ratio was 3.91:3.56. The blood urea level was 106 mg. per 100 cc., creatinine 2 mg., and sulfate 8.2 mg. The sedimentation rate was 131 mm. per hour (Westergren). There was no bilirubin on the direct test, but the indirect test revealed 1.4 mg. per 100 cc. of serum. Serologic tests for syphilis were negative. The lupus erythematosus test was negative.

Cystoscopy revealed "moderate urethritis and cystitis cystica over the base." A chest roentgenogram revealed no abnormalities. A gastric roentgenogram showed a "hiatal hernia with about one-third of the stomach above the diaphragm." Bone marrow (sternal aspiration) on volumetric study yielded 3% fat, 67% plasma a myeloid-erythroid layer of –1% and 29% erythrocytes. Examination of bone marrow smears revealed "a hypocellular marrow with lymphocytes being the predominating cell. There are a few granulocytes present, only an occasional normoblast seen and no megakaryocytes found." Fixed tissue sections of the marrow disclosed aplasia of the bone marrow, with replacement by fatty tissue.

The patient's course in the hospital for 22 days was relatively quiet, since she had neither active hemorrhage nor agranulocytic complications. The anemia, however, was troublesome. The concentration of hemoglobin fell from 11.3 gm. to 9.7 gm. to 8.8 gm. per 100 cc., on a weekly basis, while the reticulocytes ranged between 1% and 1.5%. Three blood transfusions, of 500 cc. each, were administered and the concentration of hemoglobin was 13.4 gm. per 100 cc. of blood at the time of dismissal. Cortisone was administered for two weeks without any evidence of benefit, and the woman was returned to the care of her family physician, who was to give transfusions as indicated. Four weeks after her return home she had continued on the same course, requiring transfusions to combat her anemia but otherwise doing well.

CASE 9.—In 1926, this white woman had received a diagnosis of chronic, discoid lupus erythematosus. She had been given multiple treatment, including quinine, ultraviolet light and colloidal gold. To the last of these she had reacted unfavorably. In the autumn of the year in which the diagnosis had been made, she came to the Mayo Clinic, where she spent 58 days in a Rochester hospital. On Oct. 19, 1926, results of laboratory work were reported as normal except that evidence of mild hypochromic anemia was found.

On March 12, 1928, because of a flare-up of the lupus erythematosus, the patient was readmitted to the Rochester hospital, where she remained for 49 days. At that time the laboratory findings again were normal except for anemia (the hemoglobin level was 70%). The patient had no other illness until 1934, when the cutaneous lesions of lupus erythematosus flared again. This condition waxed and waned in a mild way until her next admission.

At the time of the admission just mentioned, which was in January, 1946, the woman complained of shifting joint pains of about two months' duration, with associated afternoon fevers and night sweats. The joint pains were severe enough to keep the patient in bed. There was also a history of recurring urinary infection. It was believed at this time that she had "chronic discoid lupus erythematosus with arthritis." There was evidence of pyuria. Esch. coli were cultured from the urine and sulfathiazole, 7½ grains (0.482 gm.), was given three times a day. All symptoms improved, with clearing of the urinary infection. The patient spent 110 days in the hospital on this occasion, during which time she was given, in addition to the treatment mentioned, bismuth arsphenamine sulfonate (bismarsen®) and quinine. She received, also, two transfusions of blood of 250 cc. each.

Results of laboratory work at the time of her admission in 1946 were reported as follows:

The urine contained albumin, grade 2, pus, grade 2, and Esch. coli on culture. The hemoglobin level was 10.2 gm. per 100 cc. There were 3,250,000 erythrocytes per cubic millimeter and 5,900 leukocytes, with 33% lymphocytes, 11% monocytes, 54% neutrophils, 1% eosinophils and 1% basophils. The blood smear showed a "toxic picture." Serologic tests for syphilis were negative. A chest roentgenogram revealed no abnormality. Roentgenograms of the joints showed "rheumatoid arthritis involving most of the joints examined." The sedimentation rate was 126 mm. per hour (Westergren). The serum protein level was 6.1 mg. per 100 cc. The albumin-globulin ratio was 1.4:1 mg. per 100 cc. At the time of the woman's dismissal, there were no abnormal laboratory findings other than mild elevation of her sedimentation rate.

In 1948, at the age of 60 years, she went to her local physician because of urinary frequency and, on pelvic examination, an early squamous cell epithelioma, grade 2, of the uterine cervix, was found and was cauterized. She was then referred to the Mayo Clinic for further advice and treatment. Pelvic examination at the clinic gave no evidence of extension; consequently, treatment for the carcinoma was limited to a course of roentgen rays. Examination in the section of dermatology revealed "mild lesions of chronic discoid lupus erythematosus, with no systemic reflections." Results of general examination otherwise were not re-

markable. The patient had had no trouble with the arthritis in the two years since she had been at the clinic, but she had had recurring urinary infection, which had become more frequent and troublesome. Streptococcus faecalis was found in the urine. Therefore, calcium mandelate was administered and acidification of the urine was effected. Laboratory studies at this time revealed that leukocytes numbered 4,500, of which 50% were neutrophils. All other values were within normal range.

In January, 1949, the patient returned to have her pelvis reexamined. She related that she had had another attack of cystitis, which had persisted for 34 days before responding to treatment. On examination there was no evidence of local recurrence of the cervical carcinoma. No other examinations or laboratory procedures were carried out at that time.

In June, 1949, reexamination of the pelvis gave no evidence of recurrence of the carcinoma and the remainder of the physical examination also indicated that the patient's condition was satisfactory. An attack of cystitis again had occurred in May, 1949, and had been treated with a total of 9 gm. of aureomycin. There was still some evidence of urinary frequency and the "lupus erythematosus was the same." Laboratory examinations at this time disclosed nothing abnormal except pyuria. Results of cystoscopic examination were reported as follows: "Bladder capacity reduced. Moderate, subacute, diffuse cystitis and dilated vessels. Factitial cystitis." Local treatment for 10 days consisted of the use of suppositories of strong silver protein and instillations of 5% mild silver protein. Aureomycin was administered for five days. Much symptomatic improvement was brought about and the urine returned to normal.

Reexamination in November, 1949, gave no evidence of recurrence of the cervical carcinoma. The lupus erythematosus was the same, and the patient was having very little trouble with the cystitis. Laboratory studies again yielded values within normal limits. The patient returned again, in May, 1950, for her usual six months' reexamination, and no evidence was found of recurrence of the carcinoma. The discoid lupus erythematosus was unchanged. "A severe anemia" was found and the woman was referred to the medical section for further study. The following history was obtained:

During the last month the patient had noticed excessive fatigue as well as exertional dyspnea. She had had mild epistaxis without any previous experience of such trouble. The patient also noted that she was bruising easily and ecchymotic areas appeared spontaneously on the limbs and other parts of the body. It developed that her urinary distress had recurred and that she had been given chloramphenicol; in fact, she had been taking 1 capsule of the drug (250 mg.) every night at bedtime for the last six months. The history and results of physical examination otherwise were not remarkable. Laboratory survey revealed the following:

The hemoglobin level was 11.0 gm. per 100 cc. There were 2,960,000 erythrocytes and 4,200 leukocytes, with 62.5% lymphocytes, 3.5% monocytes, 32.5% neutrophils, 0.5% eosinophils, and 1% basophils. There were 1.1% reticulocytes and 37,000 thrombocytes. The sedimentation rate was 56 mm. per hour (Westergren). The blood urea level was 28 mg. per 100 cc. There was no serum bilirubin on the direct test, and 1.2 mg. on the indirect test. Serologic tests for syphilis were negative. A blood smear revealed anisocytosis, with scattered macrocytes, some polychromasia, neutropenia, and diminished number of thrombocytes.

There was no dye retention on a sulfobromophthalein test of liver function. Analysis of gastric content showed 56 degrees of total acidity and 36 degrees of free hydrochloric acid in a quantity of 125 cc. A roentgenogram of gallbladder revealed cholelithiasis. A roentgenogram of stomach revealed no abnormalities. Volumetric study of bone marrow material aspirated from the sternum revealed 13% fat, 57% plasma, 1% myeloid-erythroid layer, and 29% blood cells. Examination of smears of marrow revealed a "hypoplastic marrow." Results of examination of fixed tissue preparations of the marrow were reported thus: "structure of a hypoplastic marrow."

Following withdrawal of chloramphenicol, the cystitis immediately flared up but local treatment with 5% mild silver protein, with tampons of strong silver protein and procaine penicillin gave relief. Treatment recommended for the hematological condition consisted of a high protein, high vitamin diet, with intramuscular injection of 15 mg. of vitamin B_{12} twice a week.

The patient's home physician supplied the follow-up data. It is now two years since we last observed her. Following her return home, hematinics and vitamin supplements were used and all other drugs were withdrawn. Treatment with cortisone was carried on for about two months, and then was discontinued for lack of evidence of benefit. No episodes of acute bleeding occurred, however, and as the months passed, the blood values slowly returned to normal.

In July, 1951, the following values were reported:

There were 4,100,000 erythrocytes and 6,000 leukocytes, with 55% lymphocytes. There were 90,000 to 160,000 thrombocytes.

In May, 1952, the following data were reported: The hemoglobin level was 12 gm. per 100 cc. The erythrocyte count was 4,700,000 and the leukocyte count 4,000 to 6,000. There were 238,000 thrombocytes. The differential leukocyte count revealed 50 to 60% lymphocytes, and 40 to 45% neutrophils. The patient has not received chloramphenicol since 1950.

Case 10.—A white woman, 18 years of age, was admitted to the Mayo Clinic on May 8, 1952, because of severe and persistent anemia, which had necessitated repeated blood transfusions. She had had what she called "chronic sinusitis," the evidence for which seemed to consist primarily of a postnasal drip. Because of this, she had been given chloramphenicol on Dec. 11, 1950. The prescription had called for 16 capsules, and she had had the prescription refilled until, by July, 1951, she had taken about 60 capsules. By the time she had taken that many capsules, she had begun to notice that she bruised easily but, she stated, she had been rather listless and tired since April, 1951. In August, 1951, she had noticed ecchymosis in areas of slight trauma and had visited her physician. Repeated studies of the blood at that time were reported to have given evidence of a satisfactory condition. For example, the hemoglobin level was 11.35 gm. per 100 cc. There were 4,180,000 erythrocytes and 5,700 leukocytes, with 38% lymphocytes, 60% neutrophils, and 2% eosinophils. There were 317,000 thrombocytes.

Two months later (November, 1951), the ecchymotic areas still had been recurring and laboratory work had revealed slight decrease in all blood values: The hemoglobin level was then 65%. There were 3,370,000 erythrocytes, 3,800 leukocytes, and 200,000 thrombocytes.

In December, 1951, petechiae had appeared for the first time and again she had consulted her physician. At this time the blood thrombocytes had decreased to 50,000 per cubic millimeter of blood while the other blood values were about the same. The hemoglobin level was 9.3 gm. per 100 cc. The erythrocyte count was 3,450,000 and the leukocyte count 3,600, with 59% lymphocytes, 3% monocytes, and 38% neutrophils. Studies of bone marrow were made at this time, and the report indicated the presence of "hypoplastic bone marrow."

In January, 1952, reexamination of the blood yielded essentially the same results as before, except that the blood thrombocytes had decreased to 21,000. Examination of the blood in February, 1952, revealed a hemoglobin level of 8.4 gm. per 100 cc. There were 3,070,000 erythrocytes per cubic millimeter and 1,900 leukocytes with 68% lymphocytes, and 32% neutrophils. At the time of this examination the hematologist reported that some of the lymphocytes were atypical. Corticotropin was given for three weeks without noticeable improvement in the blood picture, and then its administration was discontinued.

The laboratory survey in April, 1952, resulted in the following data: The hemoglobin value was 9.4 gm. per 100 cc. There were 3,450,000 erythrocytes, and 2,800 leukocytes with 70% lymphocytes, 27% neutrophils, 2% eosinophils, and 1% basophils. There were 28,000 thrombocytes.

At this time the patient had had a massive gastrointestinal hemorrhage, with syncope, requiring hospitalization and two transfusions of blood. After that time (March, 1952), she had received a transfusion of blood every two weeks to combat her anemia. Cortisone also had been given intramuscularly three times a day for seven days, but with questionable benefit. At the time of the patient's admission to the Mayo Clinic, she was pale and her blood pressure was 80 mm. Hg systolic and 50 diastolic. Her temperature was 99 F. Scattered ecchymotic areas and multiple petechiae were noted over the lower extremities.

Results of laboratory work on this occasion were reported as follows: The urine was normal. The hemoglobin level was 7.9 gm. per 100 cc. There were 2,470,000 erythrocytes per cubic millimeter and 2,600 leukocytes, with 65% lymphocytes, 9% monocytes, 25% neutrophils, and 1% eosinophils. There were 1.3% reticulocytes and 80,000 thrombocytes. The bleeding time was 17 minutes.

The report of the blood smear read "Anisocytosis with some macrocytosis, polychromasia and basophilic stippling. Platelets are reduced. Leukopenia with relative lymphocytosis. No remarkable immaturity was evident." (One normoblast was seen.) Serologic test for syphilis was negative. A Coombs' test was negative. The serum bilirubin level by the indirect test was 0.7 mg. per 100 cc., and negative by the direct test. The prothrombin time was 19 seconds. Volumetric study of aspirated bone marrow yielded a myeloid-erythroid layer of 2%, while examination of the bone marrow smear revealed "a hypoplastic marrow with decrease in the myeloid line and only a rare immature megakaryocyte seen. The normoblastic line is abnormal in that the cells are suggestive of megaloblastic changes, many with fragmentation and karyorrhexis of nuclei. These abnormal appearing erythroid elements show much mitotic activity. Fixed preparations show little nests of these cells with many mitotic figures. Plasma cells are numerous and the fixed tissue sections show a fatty, hypoplastic structure."

A study of bone marrow on the day of dismissal, May 19, 1952, revealed a myeloid-erythroid layer of less than 1%, while examination of the bone marrow smear preparations showed, "The erythroid line is about as before while the myeloid line is depressed. There is an increase in mature lymphocytes and plasmacytes. Only one megakaryocyte could be found." The patient was returned to the care of her home physician, who has continued to administer cortisone in therapeutic doses and to give transfusions of blood as her anemia dictates. Three weeks after her dismissal from our care, her condition continued to follow the same course.

POSSIBLE MECHANISM, RAPIDITY OF EFFECTS, AND INEFFECTIVENESS OF TREATMENT

In analyzing the foregoing reports, there seem to be at least three patterns. One of these suggests a sensitivity mechanism. In four cases (cases 1, 2, 6, and 7) the initial course of treatment with chloramphenicol seemed to be unattended by ill effects, whereas the second course seemed to precipitate the failure of bone marrow. In two of these four cases (cases 1 and 2) also, there were immediate drug reactions of nausea and vomiting, followed by jaundice in case 2. Three cases in which treatment was intermittent (cases 3, 8, and 10) may well fit into the same pattern, but it was impossible to obtain a history whereby ingestion of the drug and appearance of signs and symptoms of aplastic anemia could be exactly related in time. It is worthy of note that only four capsules of the drug constituted a second course in two cases (cases 2 and 6).

Acute aplasia of bone marrow was precipitated in two cases (cases 4 and 5) by a single course of chloramphenicol. However, gradual suppression of the bone marrow may be a third mechanism. In case 9 such suppression followed daily ingestion of 1 capsule of chloramphenicol for six months and recovery eventually resulted after withdrawal of the drug. Some of the cases (especially case 8) in which treatment with chloramphenicol was intermittent, might actually belong to this group.

There was a history of previous sensitivity to penicillin in two cases (cases 2 and 7), a history of reaction to gold in case 9, a history of hay fever in case 1, and a history of vasomotor rhinitis in case 10. Perhaps, in these cases, allergic diathesis existed. Such a history should be considered important when therapeutic agents must be chosen.

It is not possible to tell from these cases whether careful hematological examinations of the patients who were receiving the drug would have forestalled the tragic complication but we think not. The dosage of the drug for most of the patients who died was figured in hours rather than in days or weeks. In most cases purpura appeared about four weeks after the beginning of the precipitating course of treatment. All fatalities were attributable to uncontrolled hemorrhage.

No treatment has been of avail in these cases. It seems that cortisone, corticotropin (ACTH), and vitamin B_{12} have had fair trials without obvious effect. Had the cases not terminated fatally in such a short time, more satisfactory evaluation of such treatment might have been possible. Repeated transfusions are indicated for supportive treatment.

ADDENDUM

Two more patients who have aplastic anemia associated with ingestion of chloramphenicol have been admitted to our hospital service since this paper was submitted for publication. Both patients are men of middle age, and the purpuric manifestations, anemia and findings relative to the peripheral blood and bone marrow are similar to those of the patients whose cases have been reported here. One man initially took only 4 capsules of the drug in treatment for a sore throat. He repeated the dose both one and two months later; thus, he took a total of 12 capsules. The other man intermittently took capsules for nine months, in treatment of a chronic infection of the urinary tract, until he had taken 160 to 180 such capsules. The bone marrow of the latter patient contained distinctly more normal cellular elements than that of the former one.

Treatment of Prostatic Cancer.—Hormonal therapy is at present the treatment of choice for the great majority of patients suffering from prostatic cancer. Remarkable relief of symptoms with regression of the local lesion and of metastases has been observed in about three-fourths of the treated cases. Many, however, soon relapse.

Statistics now indicate some increase in the ultimate survival time of patients treated by castration and estrogens. The latter are usually first used in the still localized cases without metastases, reserving orchiectomy for the patients who do not respond or in the event of a later recrudescence.

Advanced carcinoma with metastases is treated by orchiectomy combined with estrogen therapy. Experiments with bilateral total adrenalectomy in the treatment of relapsed prostatic carcinoma await the judgment of time.

The only reported cures, however, have been effected by radical surgery. Nevertheless, the over-all prognosis is discouraging, since radical prostatectomy is applicable only to a small fraction of the total number of cases. This low percentage of operability is due mostly to the advanced nature of the lesion when first detected, as well as to the age and the debilitated condition of some of the patients. Effort should be made toward early diagnosis by means of periodic rectal examination. There is doubt, however, as to whether all the small so-called "occult carcinomas" accidentally discovered and cured by radical prostatectomy are indeed biologically malignant.

Preoperative hormonal therapy may render more patients amenable to radical surgery and may thus in the future lead to a higher rate of curability.—Seymour F. Wilhelm, M.D., Carcinoma of the Prostate, *The Medical Clinics of North America*, May, 1952.

CHLORAMPHENICOL AND APLASTIC ANEMIA

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Since chloramphenicol is an efficient broad spectrum antibiotic that is widely used, the possibility that it may be the cause of hematological disorders is, naturally, a serious one. Recently, five cases of fatal aplastic anemia have come to our attention. In each instance, we believe chloramphenicol to be etiologically implicated. It is our purpose to report these cases and to review the literature on hematological disorders believed to be caused by this drug.

REPORT OF CASES

CASE 1.—A 31-year-old housewife had received phenobarbital and atropine intermittently for over a year because of nervousness. In December, 1951, an upper respiratory tract infection developed, and she was given a total of 15 capsules of chloramphenicol. Early in January, 1952, she received an additional six capsules. On this occasion, urticaria developed over the lower extremities and lasted for several days. No other recent history of exposure to drugs or toxic agents could be obtained, and the allergic history was otherwise negative. About Feb. 1, 1952, she first noticed malaise and lack of energy, and on Feb. 8, petechiae appeared on her arms and legs. She was hospitalized on Feb. 15, and pancytopenia with hypocellular bone marrow was found. The patient was transferred to the Walter Reed Army Hospital on Feb. 26.

On physical examination she appeared to be in no distress, and the only conditions of note were pallor of the skin, scattered petechiae, and several ecchymoses over the arms and legs. Laboratory tests on admission showed 3,250,000 red blood cells per cubic millimeter; hemoglobin, 9.7 gm. per 100 cc.; 3,000 white blood cells per cubic millimeter, with 88% lymphocytes, 9% segmented neutrophils, 2% monocytes, and 1% eosinophils; 0.3% reticulocytes; and 20,000 platelets per cubic millimeter. The bleeding time was 43 minutes and the coagulation time, 4 minutes. A tourniquet test was highly positive. Results of urinalysis were normal, except for a trace of albumin. A roentgenogram of the chest was normal. Two examinations of aspirated bone marrow showed an extremely hypocellular marrow consisting of about 85% adult lymphocytes. The same condition was observed in marrow slides transferred from the hospital in which the patient had been previously.

The patient was given corticotropin (ACTH), 40 mg. daily administered intravenously, and large doses of vitamin B_{12}, ascorbic acid, and vitamin K. Transfusions of freshly drawn blood (using plastic bags) were given as indicated. Because of difficulty with intravenous administration, the corticotropin therapy was stopped after four days, and cortisone, 200 mg. daily given orally in divided doses, was administered. Despite treatment, the patient's course over the next two weeks was gradually downhill. She continued to bleed vaginally after the onset of her regular menstrual period on Feb. 22. Petechiae and ecchymoses became more evident. Nine transfusions in a two week period were required to keep the hemoglobin level at about 10 gm. per 100 cc. Results of blood determinations done on March 11 were 1,900,000 red blood cells; hemoglobin, 7.4 gm. per 100 cc.; 1,450 white blood cells, with 95% lymphocytes; 0.2% reticulocytes; and 4,700 platelets. In the evening of the same day, the patient complained of abdominal distention, and within an hour the blood pressure had dropped to a shock level. Despite administration of 10 units of blood during the next 24 hours, the patient remained in shock and died on March 15, after having a short convulsive seizure.

At autopsy, numerous petechial and ecchymotic lesions scattered over the body were seen. The peritoneal cavity contained about 800 cc. of fresh blood. There was a large hematoma of the left ovary, obscuring most of the ovarian tissue. On microscopic section, the blood was seen to be coming from a hemorrhagic corpus luteum. Petechial hemorrhages were scattered throughout the white matter of the brain, the heart, gastrointestinal tract, and kidneys. The bone marrow grossly appeared pale brown and on section showed marked hypocellularity, with small foci of cells, which were mainly lymphocytes, seen only occasionally. Small foci of extramedullary hematopoiesis were seen in the abdominal lymph nodes, liver, and spleen.

Comment.—This was a 31-year-old housewife who took a total of about 5.5 gm. of chloramphenicol in two courses and in whom fatal aplastic anemia developed three to four weeks later. It is of interest that urticaria lasting several days developed when the second course was administered. The patient had had no other drugs known to cause aplastic anemia within a reasonable period prior to her fatal disorder.

CASE 2.—A 23-year-old man gave a history of having had recurrent sinusitis over a period of several years. For the first time, in November, 1951, he took 24 capsules of chloramphenicol because of an upper respiratory tract infection and sinusitis, and he took the same number again in early December. At the same time he took APC (aspirin, acetophenetidin, and caffeine) tablets, codeine, phenylephrine (neo-synephrine®) hydrochloride nose drops, and "black-colored nose drops." On Dec. 10, 1951, scattered petechiae and ecchymoses developed. Over the next two months, he noticed increasing weakness and dull frontal headaches. On Feb. 6, 1952, he had a mild epistaxis and was admitted to another hospital. Extensive studies done at that time showed pancytopenia and extremely hypocellular bone marrow on repeated aspiration. The patient stated that during this hospitalization he again received about 24 capsules of chloramphenicol because of a small ulcer on his lip. Other medication at that time consisted of analgesics for headache and ascorbic acid. Although the patient had worked in an army hospital pharmacy for 11 months previously, he denied taking any other drugs. The allergic history was negative.

On admission to Walter Reed Army Hospital, physical examination showed a fair degree of pallor and scattered petechiae over the trunk and lower extremities. Laboratory data were as follows: 1,800,000 red blood cells per cubic millimeter; hemoglobin, 6.2 gm. per 100 cc.; 1,800 white blood cells per cubic millimeter, with 10% segmented neutrophils and 89% lymphocytes; 7,500 platelets per cubic millimeter; 0.2% reticulocytes; and a hematocrit of 20%. The bleeding time was more than 16 minutes, and the clotting time was 5 minutes. A tourniquet test was highly positive. Roentgenograms of the chest, sinuses, mastoids, and abdomen were normal. Urinalysis showed many red blood cells and a few white blood cells per high power field. Aspiration of sternal marrow showed it to be extremely hypocellular, with 90% adult lymphocytes.

The patient was given cortisone, 300 mg. per day administered orally in divided dosage, vitamin B_{12}, ascorbic acid, and fresh blood transfusions as indicated. He was given penicillin, aureomycin, or terramycin during most of his hospital stay. Ten pints of blood were required to maintain the hemoglobin level at about 10 gm. per 100 cc. Gastrointestinal bleeding, high fever, jaundice, and pneumonitis developed terminally, and the patient died on May 4, 1952.

At autopsy, the skin of the entire body was moderately icteric and covered with petechiae and ecchymoses. Scattered throughout the myocardium, lungs, liver, spleen, and kidneys were large numbers of round soft white nodular areas 4 to 5 mm. in diameter. The entire gastrointestinal tract, from stomach to anus, showed myriads of similar mucosal nodules with ulcerated punched out centers. On microscopic section, these areas were observed to be large colonies of bacteria and fungi, which on culture were found to be hemolytic Staphylococcus aureus and Candida. Surrounding the colonies there was practically no in-

From the medical and laboratory services of the Walter Reed Army Hospital and the Medical Department of George Washington University Hospital. Lieutenant (MC), United States Army Reserve (Dr. Spurling).

flammatory reaction, although some necrosis was present, particularly in the liver. The lungs showed, in addition, diffuse hemorrhage and hemorrhagic infarction. There was a diffuse organizing pneumonitis. The bone marrow grossly appeared light tan in color; on section there was moderate hypoplasia, with virtual absence of granulocytic elements and megakaryocytes. The cells consisted mainly of lymphocytes and plasma cells, with a few nucleated red blood cells. Foci of extramedullary hematopoiesis were found in the liver, lymph nodes, and spleen. The spleen also showed considerable erythrophagocytosis.

Comment.—This was a 23-year-old soldier who had taken three courses of chloramphenicol for a total dose of about 18 gm. The aplastic anemia became apparent about one week after the second course, and a third course was taken during the aplastic process. Despite therapy, he died about 145 days after onset.

CASE 3.—Furuncles developed in an 18-year-old college student in the late summer of 1951. She said she had been given chloramphenicol in August, 1 capsule every 3 hours while awake for 2 weeks. The records of her physician showed that she had received a short course in June and another in July for furunculosis, with no record of any drug being taken in August. In early October, the patient first began to notice scattered ecchymoses, which continued to recur. Late in October, she had an upper respiratory tract infection and took two more capsules of chloramphenicol without the physician's advice. In late November, she first began to notice petechiae. Blood studies on Nov. 21, 1951, showed 3,800,000 red blood cells per cubic millimeter; hemoglobin, 11.6 gm. per 100 cc.; 5,100 white blood cells per cubic millimeter with 37% segmented forms, 6% band forms, 56% lymphocytes, and 1% monocytes. The platelet count was 34,200 per cubic millimeter. The patient had another furuncle about this time, which responded to hot soaks and ammonium ichtholsulfonate ("icthyol") ointment. Pallor, fatigability, and dizziness had been noticed about this time. The patient was admitted to the George Washington University Hospital on Dec. 8, 1951. Physical examination at that time revealed mild pallor, crops of petechiae, ecchymoses, and several mucous membrane hemorrhages in the mouth. Laboratory data revealed 9.7 gm. of hemoglobin per 100 cc., 2,700,000 red blood cells, and a hematocrit of 25%. The platelet count was 27,000, and the white blood cell count was 6,000, with 50% segmented neutrophils, 49% lymphocytes, and 1% monocytes. The bone marrow aspirated from the sternum had a fair number of cells with no megakaryocytes. Macronormoblasts were seen, and there was some increase in adult lymphocytes and plasma cells. The result of the van den Bergh test was normal, and that of Coombs' test was negative. There was no response to vitamin B_{12}, liver extract, or folic acid therapy, which was tried because of the macronormoblasts. Bone marrow aspiration repeated a week later showed a definite decrease in the number of cells and a further increase in the percentage of lymphocytes and plasma cells. The patient was started on corticotropin therapy, which later was changed to cortisone therapy, 200 mg. per day administered orally in divided doses, for ease of administration. From this time until her death on Feb. 27, 1951, a progressive aplastic anemia gradually developed, which was characterized by anemia, thrombopenia, leukopenia, and an aplastic bone marrow. Therapy was continued with large doses of cortisone (100 to 300 mg. per day given orally) throughout this time. The only apparent effect of this drug seemed to be suppression of bleeding, at least until the terminal complication. The bone marrow showed complete aplasia, with only lymphocytes and plasma cells remaining. Other treatment included testosterone, thyroid, vitamin B_{12}, folic acid, liver extract, and repeated transfusions as indicated. Five cubic centimeters of normal marrow injected into the patient's sternal cavity resulted in only a severe febrile reaction. Her course was marked by occasional furunculosis in the axillae, which responded to large doses of penicillin. Bleeding occurred into the skin and mucous membranes and on one occasion from the kidneys for three days. In early February, the patient had severe epigastric pain and several days later passed liquid reddish and black stools. Her final episode was an overwhelming melena that persisted for three days, with marked abdominal distention, and she finally died, despite continuous transfusions.

Comment.—This 18-year-old girl took chloramphenicol for recurrent furunculosis, and about five weeks later purpura developed. Over the succeeding months an aplastic anemia developed, and she finally died of overwhelming gastrointestinal bleeding. She had taken no other drugs previously. It is a point of issue whether the patient took additional chloramphenicol on her own initiative in August or whether the drug administered in July was the last she took prior to the development of symptoms of thrombopenia in early October.

CASE 4.—A 36-year-old white waitress was first admitted to the George Washington University Hospital on July 21, 1951, for treatment of an indolent ulcer on the medial aspect of her right ankle. This had developed several years previously following an injury and had resisted treatment since that time. Blood determinations at this admission were hemoglobin, 13.9 gm. per 100 cc.; hematocrit 46%; and leukocytes 10,450 per cubic millimeter; with 68% segmented neutrophils and 32% lymphocytes. The ulcer base cleared following aluminum acetate (Burow's) solution soaks, and granulation and healing finally occurred. During the patient's stay, a serologic test for syphilis was found to be positive. She received the following therapy: chloramphenicol, 500 mg. every 6 hours for 2 days, then 250 mg. every 4 hours for 26 days, and finally 500 mg. every 6 hours for 8 days, for a total of 61 gm.; sulfisoxazole (gantrisin®), 1 gm. every 4 hours for 9 days, for a total of 54 gm. (discontinued July 9, 1951); in addition, she received aluminum acetate solution compresses; pentamethonium chloride; phenylephrine hydrochloride nose drops; aureomycin "pharyngets," 1 every 2 hours from July 25, 1951, to Aug. 7, 1951; "vi-syneral" (a multiple vitamin preparation), intramuscularly administered; dihydrocodeinone (hycodan®) bitartrate, and lyocyte® (dried red blood cell concentrate) powder applied to the ulcer crater.

The patient was readmitted on Nov. 23, 1951, saying that she had continued taking chloromycetin for another three weeks (dosage unknown) following her discharge from the hospital. She also had had a short course of priscoline® (2-benzyl-2-imidazoline hydrochloride), which was discontinued because of gastrointestinal intolerance. She had last taken chloramphenicol near the middle of September. About 10 days before admission, she first noted petechiae and ecchymoses. Ulorrhea began three days before her admission to the hospital. Examination revealed an acutely ill woman with a temperature of 39.4 C (102.9 F). Petechiae were scattered over all the extremities, the face, and the trunk, and ecchymoses were noted on the thighs and arms. The gums were spongy, with a few small areas of necrosis. Blood determinations at that time showed 12.4 gm. of hemoglobin per 100 cc.; hematocrit of 40%, 4,300,000 red blood cells, 1,900 white blood cells, with 20% segmented neutrophils, 4% band forms, and 76% lymphocytes. Sternal puncture (and later rib puncture) revealed an extremely hypoplastic marrow infiltrated or replaced by lymphocytes and plasma cells. The platelet count was 24,720, and the bleeding time was 15 minutes. There was only slight clot retraction in 24 hours. The clotting time (3 tube Lee and White) was 15 minutes. The patient was started on terramycin and cortisone therapy. Cortisone therapy was discontinued after 11 days, because a high spiking fever developed, and it was believed a bacteremia was being masked. This was borne out by a positive blood culture of a hemolytic Staph. aureus. The patient was given large doses of terramycin, streptomycin, and penicillin. Despite antibiotic therapy, the patient's condition became increasingly toxic. Her red blood cell count, hemoglobin level, and hematocrit gradually fell, despite repeated transfusions, reaching the following low points: 7.3 gm. of hemoglobin per 100 cc., 2,550,000 red blood cells, and a hematocrit of 24%. Her white blood cell count had increased from 1,900 on admission to 7,200 during her hospital course, but the lymphocyte count remained high, and at the time of her death her white blood cell count had dropped to 950. Cellulitis of one arm, severe generalized muscular aching, bilateral chest rales, and abdominal distention developed, and the patient died, having the clinical picture of extreme toxemia.

Comment.—This was a 36-year-old woman with a chronic ankle ulcer who had a positive reaction to a syphilis test and was treated with chloramphenicol and a number of other agents. About two months after she received chloramphenicol, an

aplastic anemia became apparent. About four months prior to the onset of the aplastic process, she had received sulfisoxazole and a variety of other medicaments, including aureomycin "pharyngets" (last given three and one-half months before the onset). She had evidence of thrombopenia, leukopenia, and anemia, and died as the result of an overwhelming Staphylococcus bacteremia and toxemia. This case points up the difficulty of establishing an etiological agent, since so many medicaments had been used; however, chloramphenicol was the last agent used before her admission to the hospital, and it had been taken one and one-half to two months after any of the others.

CASE 5.—A 26-year-old white woman had had eczema and acne on her extremities and face for about two years. Her most recent treatment had consisted of chloramphenicol, four 250 mg. capsules taken daily for about two months. This was discontinued on May 18, 1952, because of nausea. On May 2, during therapy, blood tests showed a hemoglobin level of 90% and 8,950 white blood cells, with 72% segmented neutrophils. The patient felt well until about June 10, when profuse vaginal bleeding developed with the onset of her menses. She continued to have hypermenorrhea and was admitted to another hospital on June 16. She said she had had fever for several days, a sore throat, and swollen glands in her neck. She had not taken chloramphenicol previously and had a negative allergic history. She had taken no other drug in the three months preceding the onset of symptoms, except for two butabarbital (butisol®) sodium tablets the day her menses began. She had taken this drug prior to the use of chloramphenicol in an undetermined amount.

Physical examination revealed a young woman who did not appear ill. There was mild bilateral cervical adenopathy, a small amount of whitish exudate on the tonsils, and a small ecchymosis on the posterior pharynx. Her temperature was 100 F, and it varied from 100 to 103 F during her stay at this hospital. Initial blood studies revealed 1,690,000 red blood cells per cubic millimeter, 5 gm. of hemoglobin per 100 cc., 3,300 white blood cells per cubic millimeter, with 50% segmented neutrophils, 46% lymphocytes, 1% monocytes, and 3% eosinophils. The platelet count was 12,500 per cubic millimeter. Petechiae on the extremities and ecchymoses at the site of needle puncture developed during this hospitalization. The patient was given three pints of whole blood, and penicillin therapy in large doses was started. She was transferred to Walter Reed Army Hospital on June 21, 1952.

Physical examination revealed several furuncles in the left axilla, scattered petechiae on the mucous membranes and extremities, a few ecchymoses, and no enlargement of the lymph nodes, liver, or spleen. Laboratory examination revealed 3,900,000 red blood cells, 12.4 gm. of hemoglobin per 100 cc., and 400 white blood cells, with 6% segmented neutrophils and 94% lymphocytes. There were 12,000 platelets. Urinalysis showed nothing remarkable except for numerous epithelial cells. Marrow obtained by sternal puncture was extremely hypocellular, the great majority of cells being adult lymphocytes, with a few plasma cells and, rarely, normoblasts and granulocytes; no megakaryocytes were seen. The diagnosis of aplastic anemia was made.

The patient was continued on penicillin therapy with large doses. It is our intention to begin administering cortisone when her infection has been controlled. Transfusions will be used as indicated.

Comment.—This is a 26-year-old woman who took 1 gm. of chloramphenicol daily for two months for treatment of acne and eczema. Twenty three days after stopping use of the drug because of nausea, menorrhagia began. The diagnosis of aplastic anemia was made because of a pancytopenia and an extremely hypoplastic bone marrow. Her course is unknown since her condition was only recently diagnosed.

COMMENT

Four other cases of aplastic anemia believed caused by chloramphenicol have been reported. It is our understanding that reports of other cases are being readied for publication. Rich and his co-workers [1] reported the case of a 63-year-old white man who was treated for a urinary infection with chloramphenicol for about 80 days, receiving a total dose of 54 gm. Generalized purpura developed while the patient was under treatment, and shortly thereafter a complete aplastic anemia appeared. The patient died 12 days after the onset of symptoms. There were several times during the course of therapy when administration of the drug was discontinued for several days and then restarted. Loyd [2] reported the death of a 28-year-old woman who had been treated intermittently for a year with chloramphenicol for an Escherichia coli urinary infection. She then received two courses of chloramphenicol about a month apart, the first of 1.75 gm. and the second, 5.75 gm. About one and one-half months later, petechiae developed, and the patient showed evidence of a full-blown aplastic anemia. Autopsy showed widespread hemorrhage and replacement of active bone marrow by fat. Harris and co-workers [3] mention two cases of aplastic anemia in an article describing the use of chloramphenicol in the treatment of 68 patients with bronchiectasis. These cases were reported in detail by Wilson, Harris, and others.[4] In each case, aplastic anemia developed during the prolonged administration of chloramphenicol (26 and 28 weeks, respectively), with total doses of 52 and 56 gm., administered 1 gm. twice weekly. Disturbance in platelet function was first noticed. One of the patients died, while the other, at the time of the report, had a hypoplastic marrow and pancytopenia five months after the onset of the toxic symptoms. Gill [5] reported two patients treated for Salmonella infection with chloramphenicol, 250 mg. given immediately and 100 mg. every 3 hours thereafter. The first patient, who had received 6.85 gm., had a drop in the white blood cell count from 11,000 per cubic millimeter, with 42% segmented neutrophils, to 10,200, with only 9% segmented neutrophils. Administration of the drug was stopped, and five days later the patient had a white blood cell count of 9,400 per cubic millimeter, with 40% segmented neutrophils. Because of this case, the next patient was watched closely; with two days' treatment, the second patient's white blood cell count went from 7,000 per cubic millimeter, with 46% segmented neutrophils, to 5,000, with 23% segmented neutrophils. Chloramphenicol therapy was stopped, and the count rose to the previous level in several days.

Volini and his co-workers [6] reported three patients in whom toxic hematopoietic effects were seen following treatment with chloramphenicol. The first of these was a young Negro boy with typhoid, who had received a total dose of 53 gm. over a period of 18 days. Prior to treatment, his blood cell counts were normal, but after discontinuance of treatment, a red blood cell count of 850,000 per cubic millimeter and a white blood cell

1. Rich, M. L.; Ritterhoff, R. J., and Hoffman, R. J.: Fatal Case of Aplastic Anemia Following Chloramphenicol (Chloromycetin) Therapy, Ann. Int. Med. **33**: 1459, 1950.
2. Loyd, E. L.: Aplastic Anemia due to Chloramphenicol, Antibiotics & Chemother. **2**: 1, 1952.
3. Harris, M. S.; Gornell, L.; Shore, C., and Lovitz, H.: Chloramphenicol in the Control of Bronchopulmonary Suppuration, Dis. Chest **21**: 450, 1952.
4. Wilson, L. E., and others: Aplastic Anemia Following Prolonged Administration of Chloramphenicol: A Report of 2 Cases, 1 a Fatality, J. A. M. A. **149**: 231 (May 17) 1952.
5. Gill, P. F.: Agranulocytopenia Following "Chloromycetin": Report on 2 Cases, M. J. Australia **1**: 768, 1950.
6. Volini, I. F., and others: Hemopoietic Changes During Administration of Chloramphenicol (Chloromycetin), J. A. M. A. **142**: 1333 (April 29) 1950.

count of 3,200 per cubic millimeter, with 8% segmented neutrophils was found. The bone marrow showed a maturation arrest in the red cell series and a diminution of granulocyte precursors. Twenty days after stopping treatment, the values had returned to normal. Two other cases of leukopenia and neutropenia with bone marrow involvement after chloramphenicol therapy were observed. The conditions reverted to normal after several weeks.

An abstract of a paper by Lindau [7] reveals other interesting data. He gave chloramphenicol for 30 days to eight patients, seven of whom had chronic degenerative diseases. In three of these, there was an arrest of the red blood cell maturation, with an average decrease in the hematocrit of 8.6% and a definite decrease of orthochromatic normoblasts in the marrow. After these conditions returned to normal, the drug was readministered to two of the three affected patients. Again the hematocrit fell and returned to normal after administration of the drug was discontinued. Janbon and Bertrand [8] recently reported anemia complicating the use of chloramphenicol in six patients (four with brucellosis, one with typhoid, and one with tuberculosis). The total doses in these cases were 140, 120, 52, 120, 54, and 21 gm., respectively. In each patient, the red blood cell count fell by about 2 million cells per cubic millimeter during the course of therapy. Four patients responded spontaneously, one responded to vitamin B_{12} and another to folic acid. The authors felt that this anemia was of the deficiency type, with inhibition of the antianemic factor due to the action of the antibiotic on the intestinal flora.

SUMMARY

Five cases of fatal aplastic anemia in patients who had taken chloramphenicol are reported. The chloramphenicol may have been the etiological factor in the development of this disorder. The current literature is reviewed.

ADDENDUM

The patient in case 5 died after this paper was submitted for publication.

1601 Argonne Place, N. W.

7. Lindau, W.: Effect of Chloromycetin upon Erythropoiesis, read before the American Federation of Clinical Research, Atlantic City, N. J., May, 1952.

8. Janbon, M., and Bertrand, L.: L'anemie du chloramphénicol, Soc. méd. hôp. Paris 67: 990, 1951.

RELATION OF HOSPITAL ADMINISTRATORS, NURSING STAFF, AND MEDICAL STAFF

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In 1947 the President of the American Medical Association, Dr. Edward L. Bortz, on the recommendation of the House of Delegates, appointed a committee to study the nursing problem in the United States, with particular reference to the shortage of nurses. The members of the original Committee on Nursing Problems were Drs. Warren Draper, Howard Gray, Leland McKittrick, and Donald Smelzer, with myself as chairman.

I think it is fair to say that at that time the other members of the committee had only a general and not an intimate knowledge of the magnitude of the problem. I know it is more than safe to say that the chairman probably knew less about the nursing problem than any man in America. He was soon to learn far more than he had planned for or gambled on.

The study was an intensive and exhaustive one. During the year, the committee met many times with representatives of the American Nurses Association, the American Hospital Association, the American College of Surgeons, and the American Medical Association. Separate meetings were held with representatives of the various organizations, and finally representatives of all of the organizations met together. In the beginning it was quickly noticeable that there was an air of suspicion on the part of the representatives of each organization toward the representatives of the others. A humorous incident took place at one of the meetings when each group sat around a large table and did not talk to the others. Later, when it was recognized that most of the problems were common to all the groups represented and that each group had an interest, that suspicion was abolished.

Soon after the beginning of the study letters began to come in from physicians and hospital administrators condemning the actions of nurses. The tone of these letters was in general severely critical of the nurses. About this time publicity was given to the study, and then the letters from nurses began to arrive. They in turn were critical of the physicians and hospital administrators and, of course, of the committee. Some of the letters were signed and some were anonymous. There were many that were critical of the committee. In substance, they said that the committee could be better occupied by investigating the shortcomings of the members of the medical profession and leaving the nurses to solve their own problems. In both instances the attitude was due to lack of understanding. Unfortunately, I believe that some such feeling still exists among physicians, administrators, and nurses. I think, however, that it is gradually being dissipated.

In 1948 the committee made its final report to the Trustees of the American Medical Association. In the report the committee recommended that nurses be divided into two classes: (*a*) professional nurses and (*b*) trained practical nurses. The professional class was to be subdivided into college-trained nurses who would serve as educators and hospital-trained nurses who would serve as supervisory personnel. The percentages of the total of all nurses in the groups recommended were as follows: 15% were college-trained nurses, 25% were hospital-

Read at the meeting of the Catholic Hospital Association of the United States and Canada in Cleveland, on May 27, 1952.

trained nurses, and 60% were trained practical nurses. The committee also recommended that the hospital training courses for nurses be reduced to two years, and the courses for trained practical nurses to one year.

I think the greatest achievement that came as the result of the study was the ability and willingness of representatives of the three groups involved to sit in the same room around a conference table and calmly and dispassionately discuss their common problems. Prior to the appointment of the American Medical Association Committee, Dr. Hugo Hullerman of the American Hospital Association had recommended the formation of a committee representing administrators, nurses, and physicians to study the problems common to all three groups. An invitation to join this group came to the American Medical Association while the Committee on Nursing Problems was making its study. The members of our committee were unwilling to affiliate with this group until the study was completed. In 1948 the Commission for the Improvement of the Care of the Patient was formed, with six representatives from each organization on the commission. The American Medical Association was one of the member organizations, and the Committee on Nursing Problems became part of the commission. Rules for operation were written and adopted, officers were elected, and the organization became a going concern.

Progress, as was to be expected, was slow in the formative years. Now the organization is one of the very hard working organizations in medicine in this country. The commission meets twice yearly. The attendance has been excellent, and the discussions and debates have been stimulating.

The problems brought before the commission are many and varied. In the beginning, the problems were chiefly related to nursing. Now the commission studies such problems as those relating to administration, medical care, interns, pathologists, radiologists, and anesthetists. In several states committees of representatives of the three groups have been formed to discuss common problems on the state level.

Few physicians are familiar with the problems of the hospital administrator. Budgetary problems are a common headache of the administrator. The difficult personnel problem is another, personality conflicts are another, and allotment of hours of work and of work on different shifts or weekends or holidays is still another. Occasionally there is a controversy as to whether a problem is administrative or comes within the province of the medical staff.

Physicians in general are not familiar with the intricacies of nursing problems. The nursing school problem is one of the difficult ones. There are also the problems of providing nursing service in the hospital when the students are at class, and maintaining required courses to conform to state laws. The required hours for various courses and the required nursing hours per patient day must be scheduled. Budget problems must be solved, and late notices to the nursing administrator that illness will prevent working that day or evening dealt with. There is also the difficulty of getting the physicians to give lectures or bedside courses and of making physicians understand that these are absolutely necessary in the operation of an accepted nursing school.

In the same way, administrators are unable to know or to understand the problems of the medical staff. Suitable staff rooms for conferences are necessary. There must be adequate equipment for all reasonable procedures. A good library must be provided. Cooperation of the administrator must be secured in the teaching program for interns and residents. Cordial and cooperative personnel must serve in the admitting offices.

Again by the same token the nursing leaders and authorities should attempt to know the problems of the medical staff. Some of these problems are very burdensome and the responsibility is great. After all, the person who is chiefly responsible for the end result that his patient obtains is the physician. It should be determined whether there has been backbiting behind the scenes, whether the nursing leaders have been carelessly evaluating physicians to lay persons, and whether nurses have been making relatives unhappy by criticizing the ability of the attending physician.

Another delicate point is the position of the physician who has courtesy privileges but is not a member of the active staff. His position may be due to unwillingness on his part or nonacceptance of him by the regular staff. Every encouragement should be shown him by the administration and the nursing staff. The medical staff should see that he is invited to attend staff conferences so that his will be a continuing educational program. If the criticism comes from him, cordial relations can frequently be established by kindly actions of the administrator or nursing staff or members of the medical staff. If the criticism comes from the administrator or the nursing staff or the medical staff, he becomes a better physician by attending staff conferences and by being familiarized with the problems of the administrator or the nursing staff.

I feel that, whenever there is disagreement in hospitals between administrators, physicians, and nurses, they are due to lack of understanding of one group of the problems of the other. I am sure that a hospital Committee for the Improvement of the Care of the Patient would help a great deal in understanding and even in solving these problems. We are all too prone to be critical of the other fellow's shortcomings when we do not know or understand his problems. It seems to me that we will not be doing our full duty to the patient until we have set up in each hospital such a committee, bringing this advancement, and I feel it is a real advancement, directly to the patient. This hospital committee made up of representatives of the three groups would go far to aid in the solution of all of these problems. I would recommend also that the representatives be top flight persons from each group.

One of the great problems confronting the American people today is the cost of hospital care. At the turn of the century and as late as the beginning of the second decade of this century, the cost to the patient in a ward was $1 a day, in a semiprivate ward, $1.50 a day, and in a private room, $2 a day. What a sad awakening one has when he receives his hospital bill today. A two weeks' stay in a private room for a surgical patient will cost about $500.

We glibly state that the average patient now becomes ambulatory more quickly and is discharged in about eight

days, whereas before he remained in the hospital about 14 days. Obviously this is not the whole answer. Heretofore, it was the common practice of the hospital to furnish all but the most unusual and most expensive medications without charge. There was only limited use of x-rays. Laboratory work was limited and usually insignificant. Anesthetics were administered by an untrained doctor or nurse. Ether and chloroform administered by drops were about the only anesthetics used. All of this has been changed, and necessarily so.

Are we as physicians depending too much on instruments of precision? Are we depending too much on the use of x-rays in chest examinations instead of the careful use of the stethoscope? Are we asking young laboratory technicians to make our diagnoses for us? Are we placing too much reliance on intricate laboratory tests when a careful history and physical examination would give us a more reliable answer? Are we placing too much stress on basal metabolic readings when a careful history of weight gain or loss, heart rate, blood pressure readings, hair distribution, and bodily stature would give us a more reliable answer? Are we leaning too heavily on electrocardiographic tracings when a careful history and physical examination would tell us more? These are some of the questions we must ask ourselves and answer if we are to contribute to the reduction of the cost of efficient hospital care.

How many of us as physicians are familiar with the cost of the antibiotics, sulfonamide drugs, cortisone, or corticotropin (ACTH)? Have we been using these preparations carelessly or without indication? Have we been using two antibiotics that might have antagonistic effect? These also are some of the questions we must ask ourselves and answer if we are to help solve this problem. How many of us are familiar with the cost of anesthesia, blood and blood derivatives, intravenous fluids, physiotherapy, basal metabolic readings, electrocardiograms, and roentgenograms? How many of our patients are being kept in private rooms in a general hospital when they would do as well or perhaps even better in a convalescent home if they are faced with long-term illnesses at great cost to the patient and the hospital?

In the past each department in the hospital has felt that its own department was a separate department and was not the concern of the others. Now we have come to know that all departments are definitely interrelated and that the work of each department must be coordinated with the others if we are to give our patients efficient and economical care.

For a long time, I have felt that a hospital operating too far out of the red was defeating the purposes for which it was intended. When great profits are shown, that profit comes from blood. God did not intend that. At the same time, I don't think it was intended that waste or carelessness should be permitted that would incur great losses. The dangers of socialism and communism are always before us. Both begin where there is want, and are thrown out as sops to a suffering people. Both are grasped for, as a drowning man grasps for a straw, little realizing the price he eventually pays. The socialist and communist uses the cost of medical and hospital care as one of the great reasons for the adoption of this abominable philosophy.

We must find ways and means to see that our patients are given efficient medical and hospital care and that the cost is kept at a reasonable amount. If the present procedures continue, the cost of medical and hospital care will continue to increase, and the law of diminishing returns will take command. I feel that all of these problems and differences can be solved and answered by the generous cooperation of the hospital administrators, nursing staff, and medical staff. This cooperation can be accomplished, I am sure, by the formation of a Committee for the Improvement of the Care of the Patient in each hospital. It is not a new idea, but it is a practical way of helping to solve these problems. With a joint national Commission for the Improvement of the Care of the Patient functioning on the national level and with committees on state level, it naturally follows that the proper place for implementation is on the hospital level.

I would further recommend that this committee meet monthly or bimonthly and that all of the problems of major or minor importance be reviewed and recommendations made for their solution. This committee should be made up of topflight persons. The seniors and leaders in each department should participate. In this way, persons responsible for policy making could speak for their divisions. We could in this way, and probably better than in any other way, familiarize all with the problems of each toward the end of providing the best medical care for all the people.

Finally we should keep before us, always, this fact: When a husband brings his wife to the hospital, a wife brings her husband to the hospital, a father and mother bring their child to the hospital, they are giving to us, for our care the body of a loved one, life's most priceless possession. We must not fail them.

147 W. Main St.

Histoplasmosis.—The highest levels of histoplasmin sensitivity in any region in the world occur in the east-central part of the USA near the junctions of the Missouri, Mississippi, and Ohio rivers, an area in which clinical cases of histoplasmosis have been repeatedly observed. In Canada, histoplasmin sensitivity has been found only in the south-eastern provinces. A somewhat lower prevalence of histoplasmin reactors than in the USA has been reported from certain localities in Mexico, Central America, and South America; the relatively small number of histoplasmosis cases diagnosed in these areas is suggestive but inconclusive evidence of the existence of endemic centres of histoplasmosis.

There appears to be very little histoplasmin sensitivity where studies have been conducted outside the Americas. Practically nothing is known concerning sensitivity in Asia, except for two investigations in India which revealed a negligible number of reactors to histoplasmin. A great many reports covering most of the European countries have failed to demonstrate any sensitivity areas, although single, isolated cases of histoplasmosis have been diagnosed in Austria, Bulgaria, England, the Netherlands, Portugal, Spain, and Turkey. Several cases have occurred in the Union of South Africa, which appears to be an area of low prevalence of histoplasmin sensitivity, but little is known of the rest of the African continent. Three cases have been observed in Java, but no studies of histoplasmin sensitivity have yet been reported.—Alessandro Mochi, M.D., and Phyllis Q. Edwards, M.D., Geographical Distribution of Histoplasmosis and Histoplasmin Sensitivity, Bulletin of the World Health Organization, Volume 5, No. 3, 1952.

CLINICAL NOTES

EMERGENCY APPENDECTOMY IN A PATIENT RECEIVING ANTICOAGULANTS FOR MYOCARDIAL INFARCTION

Joseph B. Vander Veer, M.D.
Alan P. Parker, M.D.
and
Frank R. Boyer, M.D., Philadelphia

The present widespread use of anticoagulant drugs for treatment and prophylaxis makes it probable that an occasional patient's treatment will be complicated by the necessity for emergency operation. This subject was brought to our attention by the occurrence of acute appendicitis in a patient receiving bishydroxycoumarin (dicumarol®) for acute myocardial infarction. There was no precedent, in our experience, for the handling of such a problem. The following report gives the important details of our management and the results obtained.

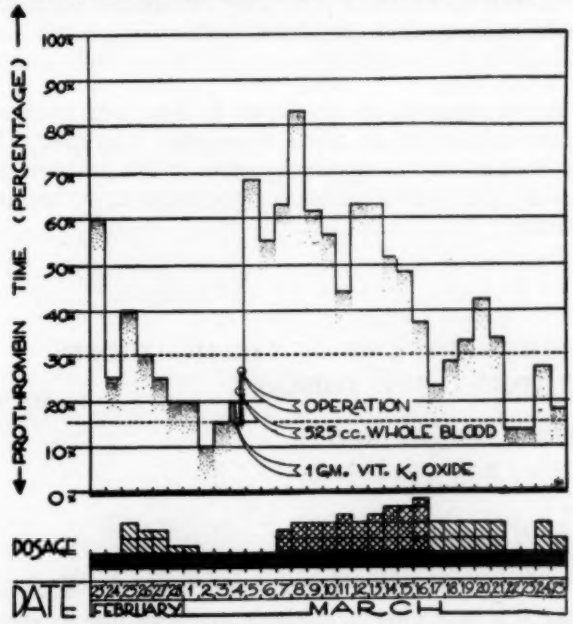
REPORT OF A CASE

T. G., a 47-year-old white man,[1] was admitted to the Coatesville (Pa.) Hospital on the morning of Feb. 19, 1951, with the diagnosis of acute coronary thrombosis. The clinical picture and course were typical, although the electrocardiographic changes were delayed. Anticoagulant therapy, with bishydroxycoumarin, was instituted on the third hospital day. Daily determinations of prothrombin time showed that an effective level of hypoprothrombinemia was maintained during the next 11 days with somewhat less than the average initial daily dosage. Fourteen days after admission, on March 4, the patient experienced diffuse abdominal pain and vomiting with gradual localization of the pain to the right lower quadrant of the abdomen. Definite localized tenderness and rigidity were present, and the diagnosis of acute appendicitis was made by the patient's family physician. After a telephone conversation with one of us (J. B. V.), who had seen the patient on Feb. 26, 1951, as a consulting cardiologist, it was decided to transfer the patient by ambulance to the Bryn Mawr Hospital for observation and possible operation (March 4). A surgical consultant confirmed the diagnosis of acute appendicitis, suspecting local peritoneal irritation, and advised immediate operation.

The prothrombin times on March 1, 2, and 3, were 20%, 10%, and 15% of normal, respectively. On the morning of the day of transfer (March 4) the prothrombin time was 20% of normal. A dose of 50 mg. of bishydroxycoumarin had been given on March 1. Because of the low prothrombin level, no bishydroxycoumarin was given on March 2 or 3. A dose of 50 mg. was scheduled for March 4, but fortunately was withheld because of the abdominal pain. Other medicaments that were given on the day of transfer were meperidine hydrochloride, 100 mg.; streptomycin, 1 gm.; penicillin, 400,000 units; and vitamin K (hykinone®), 20 mg. The last drug was given in two doses of 10 mg. each, intramuscularly, at 4 p. m. and 6 p. m.

It was decided to proceed with laparotomy after rapid preparation of the patient with vitamin K_1 oxide and citrated whole blood and, if unusual bleeding occurred in the abdominal wall, to postpone entering the peritoneal cavity until the bleeding tendency could be corrected. One gram of vitamin K_1 oxide [2] was dissolved in 25 cc. of 95% alcohol, mixed with 500 cc. of isotonic sodium chloride solution, and given fairly rapidly, starting at 9 p. m. This was followed by the administration of 525 cc. of citrated whole blood.[3] Blood for the determination of prothrombin time was taken at 9 p. m., and at 10:30 p. m., frozen overnight, and reported the following day as 15% and 24% of normal, respectively. The operation was begun at 10:45 p. m., with cyclopropane, ether, and oxygen anesthesia after intravenous thiopental sodium induction. Curare (12 mg.) aided in producing adequate relaxation. An acute gangrenous appendix without perforation was found and removed without drainage, the operation being completed at 11:50 p. m. No unusual bleeding was encountered, and no further blood was given.

Recovery from operation was relatively uneventful. The temperature reached 101.6 F within the first 24 hours after operation and gradually fell to normal during the next six days. A mixture of 400,000 units of penicillin and 0.5 gm. of dihydrostreptomycin was given intramuscularly every 12 hours for six days after operation. On the morning after operation the prothrombin time was 68% of normal. On the three following days the prothrombin times were 55%, 63%, and 83% of normal, respectively. Anticoagulant therapy was resumed on the third morning after operation, with ethyl biscoumacetate (tromexan® ethyl acetate). Despite the use of large (single) daily doses of this drug, the prothrombin time did not fall to an effective anticoagulant level during the next 10 days (see the accompanying figure). When bishydroxycoumarin was substituted, it was found that doses much larger than average were needed to produce effective prothrombin levels. This seems significant in view of the less than average doses of this same drug needed to produce the same levels preoperatively.



Serum prothrombin time (percentage) in patient T. G., before and after operation. Each square of diagonal lines indicates 50 mg. of bishydroxycoumarin. Each cross hatched square indicates 300 mg. of ethyl biscoumacetate. The broken lines mark the therapeutic anticoagulant zone.

COMMENT

The problem of surgery in a patient receiving full anticoagulant (bishydroxycoumarin) therapy (prothrombin time, 15% to 20% of normal) was handled empirically and without the benefit of immediate prothrombin time determinations. The good results obtained may have been at least partially due to the fact the patient had had no anticoagulant drug for three days prior to operation. Nevertheless, it would seem that the vitamin K (synthetic), Vitamin K_1 oxide, and citrated whole blood, which were given just prior to surgery, were effective in preventing any abnormal bleeding. The relative efficacy

From the Medical and Surgical Services of the Bryn Mawr Hospital, Bryn Mawr, Pa.

1. Dr. Julius Margolis provided the data for this patient and gave permission to publish the report.
2. The vitamin K_1 oxide used was furnished by Merck & Company, Inc., Rahway, N. J.
3. The blood was obtained from the hospital blood bank and was approximately 48 hours old.

of these different substances cannot be determined in this instance. Our previous experience leads us to believe that the use of the vitamin K_1 oxide was probably an effective measure. The fact that citrated whole blood was given just before the operation must not be overlooked, however.

Prior to operation, somewhat less than average doses of bishydroxycoumarin were needed to produce an effective prothrombin depression. After operation anticoagulant therapy was again resumed, with ethyl biscoumacetate. Unusually large doses were used, and an effective level was not reached in 10 days. Resumption of bishydroxycoumarin therapy demonstrated the fact that the doses needed to produce equal prothrombin depression were much greater than in the preoperative period. The question may be raised whether the vitamin K_1 oxide therapy and/or the blood transfusions may have been operative in producing the relative resistance to the anticoagulant drugs postoperatively.

SUMMARY

Acute appendicitis developed in a patient receiving anticoagulants for an acute myocardial infarction. The methods utilized in the management of this problem, including preoperative and postoperative care, are described.

330 S. 9th St.

SHORT-TERM USE OF CORTICOTROPIN AS ADJUNCTIVE THERAPY

William S. Reveno, M.D.
Herbert Rosenbaum, M.D.
and
John H. Buell, M.D., Detroit

As experience with corticotropin (ACTH) accumulates, it is becoming increasingly apparent that its greatest usefulness is less as a cure in disease states than as an antitoxic agent, bolstering the defense mechanism and promoting remission. This quality may assert itself by the liberation of substances that absorb toxins by strengthening the cell membrane to prevent entry of damaging agents or by preventing disorganization of enzymatic processes within the cell itself. Bacterial growth is not inhibited, and specific antibody formation is neither accelerated nor arrested. The action may be presumed to be mainly one of blocking the action of toxins and allowing an adequate build-up of the defensive processes.

Viewed in this light, the potentialities of the short-term use of corticotropin for conditions in which there is poor response to other therapy becomes readily evident. Systemic infections, shock states, and acute toxemias, when the patient is overwhelmed or floundering, may be brought under control by the addition of this protective agent, as is illustrated in the following instances.

CASE 1.—J. S., a 63-year-old man, was admitted to the hospital on May 16, 1951, with a diagnosis of acute appendicitis and peritonitis. At operation a ruptured gangrenous appendix with purulent peritonitis was found. The appendix was removed, the wound closed, and a cigarette drain placed in the fascial layer. One-half gram of streptomycin and 300,000 units of procaine penicillin were given intramuscularly twice daily. The abdomen remained distended, and the patient started hiccoughing on the second day. The temperature was elevated to 100 F, and the pulse rate ranged from 110 to 120 per minute. Attempts at passing a Miller-Abbott tube were unsuccessful, and the patient was becoming increasingly toxic and exhausted. While administration of the antibiotics was continued and the daily salt intake reduced, 20 mg. of corticotropin was injected at 10 a. m. on the third day and 10 mg. given every 4 hours, for a total of 12 doses in 48 hours. Six hours after the initial dose, flatus was passed for the first time, and the abdomen was less distended. The temperature dropped to 98.8 F, the pulse rate to 100, and the patient was more comfortable. On the following morning he had a liquid bowel movement, with further reduction in the distention; the temperature remained normal, and the pulse rate dropped to 86. The patient took food with relish and appeared much less toxic. The next day he was even more improved, had another liquid movement, and was passing flatus freely; the distention was practically gone. The hiccoughing had now stopped. Improvement continued from this day on, and he was discharged on the 14th day, having made an uncomplicated recovery.

CASE 2.—R. J., a white man, 61, was admitted to the hospital May 18, 1951, with a diagnosis of acute diverticulitis with perforation and generalized peritonitis. Severe pain in the left lower quadrant of the abdomen and temperature of 101.4 F had occurred the evening before. The fever had persisted, and the abdominal tenderness was now marked over the entire lower part of the abdomen.

Conservative therapy was instituted. Continuous tube suction was started, succinylsulfathiazole (sulfasuxidine®) and terramycin were given by mouth, and penicillin and streptomycin injected intramuscularly. The temperature remained elevated during the next week, and it became evident that an abscess had developed in the left lower part of the abdomen. While this area was palpated, the abscess ruptured, and the patient was taken to the operating room, where the abscess was drained and three Penrose drains left in situ.

In spite of seemingly adequate drainage and continued treatment with antibiotics, the temperature and pulse rate remained elevated, and the patient was making no progress. On the fifth day an injection of 20 mg. of corticotropin was given, followed by a 10 mg. dose every four hours for a total of 12 doses. Six hours after the first injection the temperature dropped to normal, and the patient reported an increased sense of well-being. He improved rapidly from this point and was discharged on June 4th, nine days after operation.

CASE 3.—A. B., a white man, 65, was admitted to the hospital April 20, 1951, because of severe knife-like pain in the right side of the chest of one week's duration. The night before admission he had a slight chill, and the pain became much severer. The temperature was 100.2 F, the pulse rate 100, and there was evidence of pleural effusion over the right lung base. There was very little cough and no hemoptysis. The white blood cell count was 10,600, with 79% polymorphonuclears, 9% lymphocytes, 9% mononuclears, and 3% eosinophils. X-ray study on April 21 showed evidence of right lower lobe pneumonia with associated effusion.

On April 21 and 22 the pleuritic pain became more intense, dyspnea was marked, and there was slight cyanosis. Strapping of the chest made the pain worse, and intercostal nerve block produced only temporary relief. Thoracentesis was done on April 23d, and only 15 cc. of cloudy orange-colored fluid was obtained. This showed principally mature polymorphonuclears, with many very large and often multinucleated histiocytes. Blood and pleural fluid culture showed no growth. Dulness was now present over both lung bases, and the pain, dyspnea, and cyanosis, with elevated temperature, persisted in spite of continuously administered oxygen and frequent use of anodynes. Use of penicillin and streptomycin, 300,000 units and 0.5 gm. respectively, was started twice daily.

On April 24, with the condition and treatment unchanged, the first injection of 20 mg. of corticotropin was given, and this was repeated every four hours for 12 doses. Six hours after the first dose the pain had stopped, the respirations had slowed, and their depth had increased. By the next morning improvement

From the Departments of Medicine and Surgery, Harper Hospital.

was even more marked; the temperature was normal, the breath sounds over the lung bases were louder, and crepitant rales were heard for the first time. There was no more dyspnea or pain during the period of corticotropin administration, but five hours after the last dose was given the pain and dyspnea recurred. Corticotropin was given again, this time in a dosage of 20 mg. every six hours, and again there was dramatic disappearance of the disturbing signs. Use of the drug was continued for the next six days at the same dosage level; administration was decreased on the seventh day to 15 mg., on the eighth day to 10 mg., and on the ninth day to 5 mg. every six hours, then discontinued. This time the improvement persisted, and, while there were occasional fleeting chest pains, the signs of effusion gradually disappeared.

X-ray studies on April 28 showed increased fluid in the basilar section of the right thorax, obscuring the lower part of the right lung. Two days later an area of consolidation was evident, which surrounded pleural thickening of the right lower lung field highly suggestive of infarct. After another four days the localized area of consolidation just above the right leaf of the diaphragm again showed no change. One area of rarefaction, without definite fluid level, was seen within the center of the lesion. The left costophrenic angle was now obliterated, suggesting accumulation of fluid here. A final x-ray on May 11 showed slight progress in resolution of the lesion in the lower third of the right lung.

On May 7, four days after use of corticotropin was discontinued, marked pain and tenderness in the calf of the left leg developed, and bilateral femoral vein ligation was performed by Dr. E. A. Osius. Recovery from the operation was uneventful, the chest signs continued to improve, and the patient was discharged May 14, 1951, 25 days after admission.

SUMMARY

In the first two patients, both with purulent peritonitis, response to therapy was indifferent and little, if any, progress was being made toward recovery. Administration of corticotropin (ACTH) for 48 hours, while use of antibiotics was continued, provided the necessary stimulus that tipped the scales toward a prompt favorable outcome. The third patient, with severe pain, dyspnea, and toxemia from pulmonary infarction, responded promptly to 48 hours' treatment with corticotropin but showed return of symptoms when it was stopped. The condition improved and recovery followed when the corticotropin therapy was resumed and continued for another six days. Accordingly, in these three patients, the value of the short term use of corticotropin for conditions in which there is poor response to other forms of therapy has been demonstrated.

968 Fisher Bldg. (Dr. Reveno).

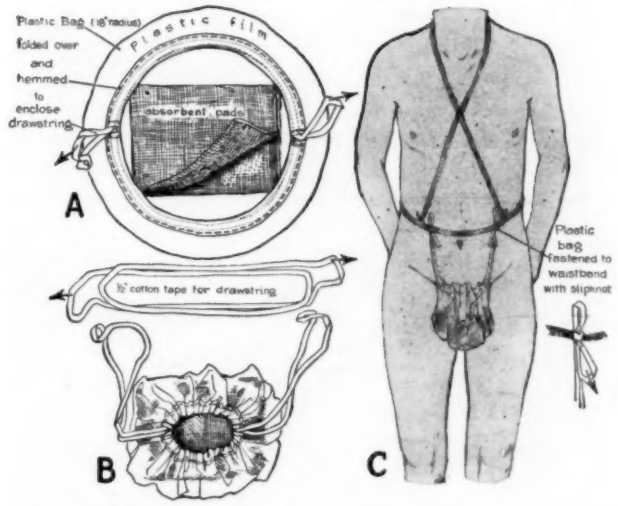
Meaningless Phrases.—In its proper proportion description of a disease entity is only the first step, and a small one at that, toward understanding of etiology, pathogenesis, and treatment. There is no disease which is thoroughly understood; often specific therapy does more to stifle progress in this respect than any other single factor. Insulin effectively stopped research on the etiology and pathogenesis of diabetes for twenty years; the antibiotics may be doing the same for infectious diseases. Medical science, still in its childhood, continues to describe new disease entities, which is progress. But when we are tempted to use meaningless phrases, or what is worse, the names of men, as descriptions, we are taking semantic refuges from the realities of ignorance. "Essential" hypertension, idiopathic thrombocytopenia, Loeffler's syndrome are examples. "Essential" means "I don't know." I have always preferred the word "agnogenic," which really says, "I don't know." Let us not be afraid to admit our ignorance, and qualify words with that humble admission, thereby making a challenge of a refuge.—Henry A. Schroeder, M.D., Knowledge, Faith and Humility, *The Centaur of Alpha Kappa Kappa*, May, 1952.

PLASTIC BAG FOR URETHRAL LEAKAGE CONTROL AFTER PROSTATECTOMY

Thomas S. Cullen, M.D., Baltimore

In March, 1950, Dr. Howard C. Smith removed the central lobe of my prostate at the Church Home and Hospital. He described it as the largest central lobe he had ever encountered in surgery; the weight was 254 gm. The posterior incision healed by first intention; nevertheless, there was a great amount of leakage from the urethral orifice, evidently due to laxness after removal of the large tumor.

As soon as I was well enough, Mrs. Cullen, a graduate of the Johns Hopkins Hospital School of Nursing, undertook control of the leakage. She selected a waterproof plastic,[1] so soft that it could hardly be felt. She made a round bag of this material sufficiently large to contain the genitalia, with a wide hem through which to draw tapes.



A, top view of plastic bag showing placing of drawstrings and absorbent pads. *B*, drawstrings drawn tight so that the bag would completely cover the genitalia. (The tighter the strings are drawn, the better.) *C*, bag in place. To prevent the bag from slipping down in the back, the two ends of the drawstrings should be fastened laterally, as far as possible, instead of near the front as indicated in the drawing.

Two absorbent pads were placed in the bag, the bag was placed around the genitalia, and the tapes were drawn tight enough to prevent leakage. Each tape string was then tied to the side of the abdominal girth (made of gauze bandage) by slipknots, which could be easily untied. The girth was held firmly by another gauze bandage placed around the neck, crossed over the chest, and tied on each side of the girth (see figure).

The plastic bag can be removed whenever necessary, usually every two or three hours during the day, and replaced by a fresh one with dry pads. At night, a urinal may be used when required. When the patient gains strength, he can remove and replace the bag without assistance.

20 Eager St. (2).

1. Acor plastic film, a product of Acor Plasticover Co., New York.

TORULOSIS (CRYPTOCOCCOSIS) PRODUCING A SOLITARY PULMONARY LESION

REPORT OF A FOUR YEAR CURE WITH LOBECTOMY

Morris Berk, M.D.
and
Bruno Gerstl, M.D., Oakland, Calif.

Torulosis, or cryptococcosis, is an often fatal disease due to a yeast-like organism and having a predilection for the central nervous system, with the lungs as the second commonest site of involvement. It has been considered a rare disease, but many cases are probably overlooked, owing to the lack of its consideration in the differential diagnosis, failure to culture the organism on suitable mediums for sufficiently long periods of time, and frequent confusion of the organism with lymphocytes or red blood corpuscles in the spinal fluid.[1] Notwithstanding, a total of nearly 200 cases have now been reported.[2] Of this number, only five cases of solitary lung involvement are on record (see the accompanying table).[3] To this meager group we add a sixth, which is considered worthy of publication not only because of its rarity but also because it simulated tumor of the lung, eventually leading to thoracotomy. Other authors have mentioned similar experiences.[4] For this reason attention is hereby again directed to the necessity for consideration of torulosis in the differential diagnosis of circumscribed pulmonary lesions. Also, inasmuch as there is no specific therapy and since pulmonary involvement may actually precede dissemination, there is a growing tendency to consider surgical resection in all cases of pulmonary cryptococcosis. Thus, Taber [4b] has stated that "the early surgical removal of a circumscribed area of torulosis seems as logical as the early removal of carcinoma." Our case would tend to bear this out.

Cases of Solitary Pulmonary Cryptococcosis Found in the Literature

Author	History	Roentgen Findings	Method of Diagnosis	Outcome and Comment
Sheppe [3a] (1924).....	Age 50; white male; 4-month illness with tonsillitis, neck stiffness, and weight loss; eventual development of signs of consolidation at right lung base	Initial x-ray normal (no additional x-rays)	Culture of pulmonary tissue at necropsy	Death; brain and meninges apparently not examined; no report of spinal fluid examination
Hardaway and Crawford [3b] (1935).	Age 33; white male; cough only symptom	Multiple nodular lesions; 15-mo. follow-up disclosed little change	Smear and culture of sputum	No essential change during 15-mo. observation
Greening and Menville [3c] (1947).....	Age 24, Negro; chest pain, cough, and hemoptysis	Patchy consolidation of upper lobe of left lung and enlargement of bronchopulmonary lymph nodes; confluence of patchy areas with cavity formation and pleural effusion; fibrosis one year after onset	Smear and culture of pleural fluid	Eventual improvement with potassium iodide, antibiotic, and roentgen therapy; alive after one year
Moody [3e] (1947).....	Age 38, Mexican; suspected tuberculosis; bronchoscopy revealed "tracheal tumors"	Submiliary lesions	Culture of tissue at necropsy	Asphyxial death
Frolo and Bailey [3d] (1949).....	Age 19; asymptomatic pulmonary lesion discovered by x-ray at Army induction; referred to tuberculosis sanitarium (negative findings); eventual pneumonectomy for possible bronchogenic cancer	"Mass-like" lesion in lower lobe of right lung	Histological examination of surgical specimen	Circumscribed, rubbery lesion, 4.5 cm. in diameter; alive 5 yr. 7 mo. after surgery without dissemination or recurrence

REPORT OF A CASE

A 30-year-old white World War II veteran, who was receiving compensation for bronchial asthma, was admitted to the Veterans Hospital, Oakland, Calif., on Oct. 31, 1947. Since 1944, when on the island of New Britain in the Southwest Pacific, he had been having infrequent episodes of cough, fever, substernal tightness, wheezing, night sweats, and malaise. He was given a medical discharge from the Army in March, 1945, with a diagnosis of bronchial asthma. After discharge and until his present hospitalization, he had several additional episodes. They were nonseasonal, and each lasted about a week. Five months prior to this hospital entry, during a health survey, a roentgenogram showed a "spot" in the left lung. He was referred to his private physician and eventually to this hospital. The patient, however, was asymptomatic until three days before hospitalization, when he noted the onset of pleural pain over the left side of the chest, malaise, feverishness, and dry cough. There were no chills, hemoptysis, or weight loss. He had had dengue while in the Southwest Pacific in 1943 and seasonal rhinitis since 1945. A maternal grandparent had asthma. There was no history of tuberculosis or of exposure to it.

Physical examination revealed a moderately ill, robust-appearing, white man with a moderate, dry, hacking cough. Respirations were not labored or wheezy. There was no cyanosis or clubbing of the fingers. Oral temperature was 100 F. The pulse rate was 96, respiratory rate 24, and blood pressure 120/88. There were no meningeal signs, skin lesions, lymphadenopathy, or hepatosplenomegaly. The percussion note was resonant throughout. Breath sounds were essentially normal, except at the left lower portion of the chest anteriorly and the lower axilla, where numerous medium and fine rales were heard. No alteration of fremitus or voice sounds was noted.

Laboratory Data.—The white blood cell count was 18,700, with 72% polymorphonuclear cells, 9% stab forms, and 4% juvenile forms. The red blood cell count was 4,700,000, with 14.3 gm. hemoglobin per 100 cc. The sedimentation rate was 95 mm. (Westergren). Results of examination of the blood for cold agglutinins were negative. Results of liver function tests were normal. Blood culture was sterile. Concentrated sputum collections and gastric wash were negative on smear and culture and in a guinea pig test for tuberculosis. The coccidioidin skin re-

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Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

1. Gendel, B. R.; Ende, M., and Norman, S. L.: Cryptococcosis: Review with Special Reference to Apparent Association with Hodgkin's Disease, Am. J. Med. **9**: 343-55 (Sept.) 1950.

2. Cook, A. W.: Cryptococcus (Torula) Meningitis, J. A. M. A. **146**: 1105-1107 (July 21) 1951.

action was negative; a test with second strength purified protein derivative yielded a positive result. Bronchoscopy disclosed a normal condition throughout, and bronchial secretions were negative for tumor cells. The initial chest x-ray (fig. 1) revealed a density occupying the anterolateral and lower portions of the upper lobe of the left lung, just above the interlobular fissure. A

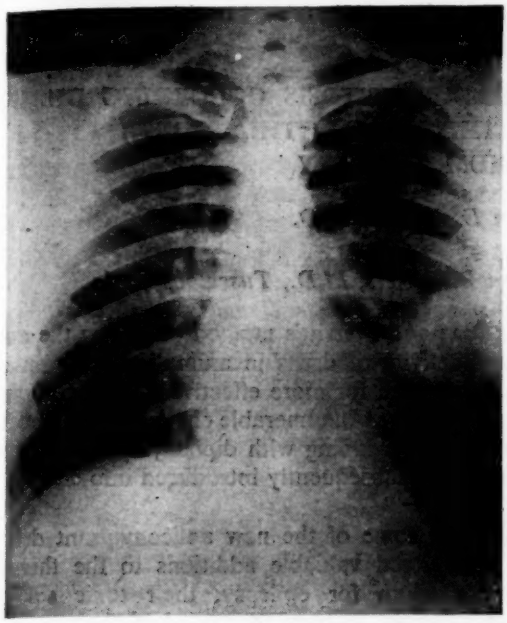

Fig. 1.—Initial roentgenogram, showing circular density in left mid-lung field.

subsequent x-ray revealed some increase in size of this shadow, with the addition of a small amount of pleural fluid (fig. 2). Bone survey and excretory pyelograms were normal, a bronchogram of the left side showed moderate cylindrical bronchiectasis in

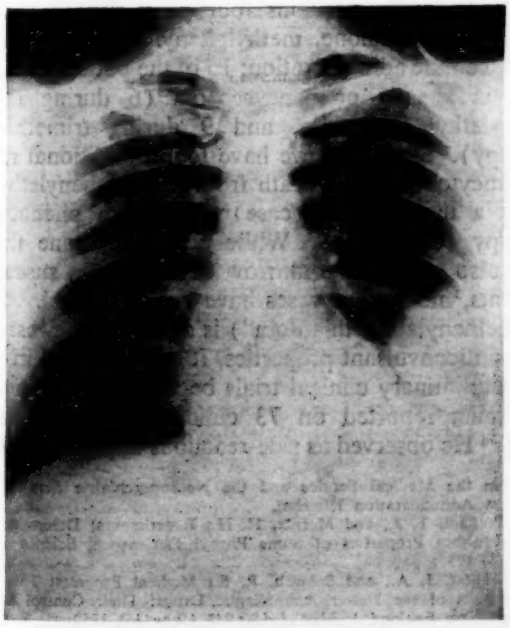

Fig. 2.—Roentgenogram taken 10 days after the first (fig. 1), with more circumscribed outline of the density and the addition of pleural effusion.

the lingular region. However, bronchi extending to the lesion in question appeared normal.

Clinical Course.—A tentative diagnosis of pneumonia was made, and the patient was treated with penicillin and sulfadiazine but without response. He continued to have fever, his temperature ranging from 99 to 101.6 F. On the eighth day after entry there was a sudden increase of pain in the left lateral portion of the chest, with physical signs of fluid, accompanied by a pleural friction rub. By thoracentesis 200 cc. of serosanguineous fluid was removed. The sediment of this fluid showed numerous cells of endothelial character. In view of the lack of response to chemotherapy with progression of the lesion seen on x-ray, the case was reviewed by the tumor board, and surgical exploration was advised. A tentative diagnosis of tumor was made. Thoracotomy was performed by Dr. David Dugan, consulting chest surgeon, five weeks after the patient's admission to the hospital, and a large tumor mass in the upper lobe of the left lung was removed by lobectomy. The tumor on frozen section was diagnosed as mycotic granuloma. The patient made an uneventful postoperative recovery and was discharged approximately two weeks later. He was still living, without evidence of recurrence or dissemination of his disease, four years later.

Description of Specimen.—Gross: The pleura of the removed upper lobe of the left lung was intact except over an oval-shaped area of the lower lateral segment, which had a dull yellow appearance. Sectioning revealed an oval-shaped, firm, tumor-

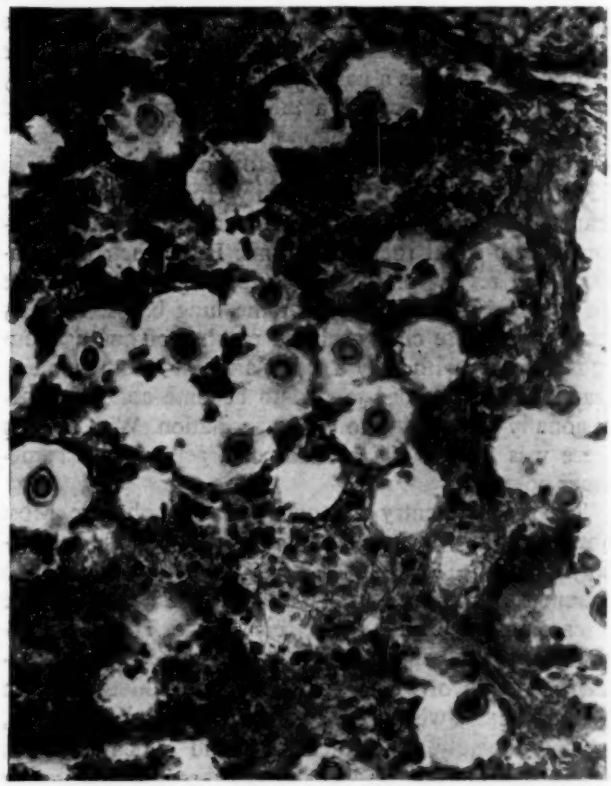

Fig. 3.—Cryptococcus organisms in lung lesion, with characteristic structure and wide refractile capsule (× 230).

like, fairly well-encapsulated, grayish yellow mass with a mucoid surface. It measured 7 by 6 by 6 cm. and corresponded in location to the pleural lesion. The remaining pulmonary parenchyma was unremarkable.

Microscopic: Sections representing the peripheral areas of the lesion revealed fairly dense connective tissue infiltrated by small round cells. The adjacent alveoli were compressed. In

3. (*a*) Sheppe, W. M.: Torula Infection in Man, Am. J. M. Sc. **167**: 91-108 (Jan.) 1924. (*b*) Hardaway, R. M., and Crawford, P. M.: Pulmonary Torulosis: Report of Case, Ann. Int. Med. **9**: 334-340 (Sept.) 1935. (*c*) Greening, R. R., and Menville, L. J.: Roentgen Findings in Torulosis: Report of Four Cases, Radiology **48**: 381-388 (April) 1947. (*d*) Froio, G. F., and Bailey, C. P.: Pulmonary Cryptococcosis: Report of Case with Surgical Cure, Dis. Chest **16**: 354-359 (Sept.) 1949. (*e*) Moody, A. M.: Asphyxial Death due to Pulmonary Cryptococcosis: Case Report, California Med. **67**: 105-106 (Aug.) 1947.

4. (*a*) Froio and Bailey.[3d] (*b*) Taber, K. W.: Torulosis in Man: Report of Case, J. A. M. A. **108**: 1405-1406 (April 24) 1937. (*c*) Dormer, B. A.; Friedlander, J.; Wiles, F. J., and Simson, F. W.: Tumor of Lung Due to Cryptococcus Histolyticus (Blastomycosis), J. Thoracic Surg. **14**: 322-329 (Aug.) 1945.

some areas the parenchyma, including blood vessels, had undergone necrosis. There were cellular debris and fine pink-staining fibers with numerous circular clear spaces. Many of the latter contained round bodies whose centers stained grayish pink and which were highly refractile. Their light pink broad peripheral zone suggested capsule formation (fig. 3). Two nearby bronchial lumina were largely occluded by granulation tissue containing a few multinucleated giant cells. With Kernohan's method,[5] the micro-organisms stained bright pink with pale yellow in the periphery. Sabouraud's medium was inoculated with fresh tissue but remained sterile. India ink preparations of imprints demonstrated a thick capsule.

COMMENT

A review of the literature shows the frequency with which pulmonary cryptococcosis presents itself as a circular, circumscribed density, usually associated with meningeal involvement, or occasionally just preceding such involvement.[6] Pulmonary lesions are said to occur in two forms: either as gelatinous masses or as fibrotic granulomatous lesions. In the first type there is massive proliferation of cryptococci into a gelatinous mass. In the second type there is a paucity of organisms. The miliary nodule, which resembles a tubercule both grossly and microscopically, is the commonest pathological lesion.[7] Greening and Menville [3c] found four cases of torulosis in 537,135 admissions to the Charity Hospital in New Orleans. In three there was pulmonary involvement, followed with serial roentgenograms. From their observations and review of the literature, they noted that the disease had a predilection for the lung bases. In early cases there were circumscribed patches of homogenous consolidation with only a small amount of surrounding reaction. These areas tended to become confluent, occasionally progressing to cavity formation. With healing there was fibrosis. Slight hilar enlargement was sometimes noted.

The portal of entry of torulosis is as yet obscure. Most observers consider it to be the lung. The disease is probably carried to other organs via the blood and lymph channels. Wade and Stevenson's [8] work indicates that the disease passes through a septicemic stage. They were unable to produce central nervous system involvement without visceral involvement (chiefly lung and kidney) when they inoculated white mice intracerebrally, intravenously, intraperitoneally, intratracheally, and subcutaneously. Intranasal inoculation caused only severe rhinitis or sinusitis. Organisms spread out beneath the cribriform plate but did not invade the central nervous system. These studies suggest initial pulmonary involvement and thus the probable importance of early resection.

SUMMARY

A case of solitary pulmonary torulosis simulating tumor is hereby added to the literature as the sixth case on record. The patient is alive, without recurrence or dissemination of the disease, four years after lobectomy. The lung may be the portal of entry of this highly fatal disease. For this reason, surgical excision is recommended as a curative measure prior to dissemination. Torulosis should be considered in the differential diagnosis of circumscribed nodular pulmonary lesions.

13th and Harrison Streets.

5. Kernohan, J. W.: A New Staining Method to Demonstrate Pathogenic Yeasts and Fungi, J. Neuropath. & Exper. Neurol. **2**: 95-98 (Jan.) 1943.

6. Hardaway and Crawford.[3b] Greening and Menville.[3c] Froio and Bailey.[3d] Taber.[4b] Ratcliffe, H. E., and Cook, W. R.: Cryptococcosis: Review of Literature and Report of Case with Initial Pulmonary Findings, U. S. Armed Forces M. J. **1**: 957-969 (Sept.) 1950.

7. Voyles, G. Q., and Beck, E. M.: Systemic Infection Due to Torula Histolytica (Cryptococcus Hominis): Report of Four Cases and Review of Literature, Arch. Int. Med. **77**: 504-515 (May) 1946.

8. Wade, L. J., and Stevenson, L. D.: Torula Infection, Yale J. Biol. & Med. **13**: 467-476 (March) 1941.

AGRANULOCYTOSIS OCCURRING DURING PHETHENYLATE ("THIANTOIN") SODIUM THERAPY

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and
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Putnam and Merritt's method of testing the anticonvulsant activity of drugs in animals opened an era of intensive search for more effective drugs with which to control epilepsy.[1] Innumerable chemical substances were tested, and, beginning with diphenylhydantoin sodium, several were subsequently introduced into clinical practice.

Whereas some of the new anticonvulsant drugs are now considered valuable additions to the therapeutic armamentarium for epilepsy, their toxic side-effects create a certain amount of hazard in the treatment of this disease. There have been reports of the occurrence of bone marrow depression, exfoliative dermatitis, nephrosis, and hepatitis, with recoveries and fatalities. Apparently depression of the blood elements is the commonest among these serious complications. In 1950, Abbott and Schwab noted that there had been 25 fatal reactions in the previous four years, which occurred during trimethadione, methylphenylethyl hydantoin, or phenacemide administration; 15 of the patients died with aplastic anemia or pancytopenia (6 during methylphenylethyl hydantoin, and 9 during trimethadione therapy).[2] Since then we have found additional reports of pancytopenia and death from methylphenylethyl hydantoin therapy (one case)[3] and from phenacemide therapy (two cases).[4] While paramethadione therapy may also cause bone marrow depression in susceptible patients,[5] no serious cases have been reported.

Phethenylate ("thiantoin") is one of the newest drugs with anticonvulsant properties. It was prepared in 1941, and preliminary clinical trials began in 1942. In 1947, Peterman reported on 73 children treated with this drug.[5a] He observed as side-reactions hypertrophy of the

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1. Putnam, T. J., and Merritt, H. H.: Experimental Determination of Anticonvulsant Properties of Some Phenyl Derivatives, Science **85**: 525 (May 28) 1937.

2. Abbott, J. A., and Schwab, R. S.: Medical Progress: The Serious Side Effects of the Newer Antiepileptic Drugs: Their Control and Prevention, New England J. Med. **242**: 943 (June 15) 1950.

3. Hofstatter, L.: Mesantoin in the Management of the Hospitalized Psychotic Epileptic: Report of Toxic Effects and One Fatality, South. M. J. **44**: 827 (Sept.) 1951.

4. Forster, F. M., and Frankel, K.: Fatal Aplastic Anemia During Anti-Convulsant Therapy, Dis. Nerv. System **10**: 108 (April) 1949. Simpson, T. W.; Wilson, E. B., Jr., and Zimmerman, S. L.: Fatal Aplastic Anemia Occurring During Anticonvulsant Therapy: Probable Idiosyncrasy to Phenurone, Ann. Int. Med. **32**: 1224 (June) 1950.

5. (*a*) Peterman, M. G.: Epilepsy in Childhood: Newer Methods of Diagnosis and Treatment, J. A. M. A. **138**: 1012 (Dec. 4) 1948. (*b*) Forster, F. M., and Borkowski, W. J.: Paradione in the Treatment of Petit Mal Epilepsy, Am. Pract. & Digest Treat. **1**: 406 (April) 1950.

gums in two cases, ataxia in four cases, and rash caused by the drug in two cases. The drug has been used in over 40 cases at the Illinois Neuropsychiatric Institute without any notable blood changes.[6] In 1950, Best and Paul reported a case of severe hypoplastic anemia with recovery occurring during diphenylhydantoin sodium, methylphenylethyl hydantoin, and phethenylate administration.[7] In 1951, Weiss and Hawley described a case of fatal pancytopenia following the use of methylphenylethyl hydantoin and phethenylate.[8] The part that phethenylate played in the production of these toxic accidents cannot definitely be stated, since in both cases this drug was given simultaneously with methylphenylethyl hydantoin, a known depressant of the hematopoietic system. In order to furnish the first known direct evidence of toxic effects of phethenylate on the bone marrow, we consider it of interest to report a case of agranulocytosis in a patient during administration of this drug.

REPORT OF A CASE

E. J., a 37-year-old divorced woman, was admitted to the neuropsychiatric service on Aug. 17, 1951. She had a history of life-long inadequacy and dependency. The onset of her psychosis was insidious and extended over a period of years. On admission, the physical examination showed nothing essentially abnormal. A routine blood cell count showed 4,500,000 red blood cells, 12.5 gm. of hemoglobin, and 5,400 white blood cells, with a differential count of 62% neutrophils, 3% eosinophils, and 35% lymphocytes. Psychiatric observation revealed that the patient was actively hallucinating; she was confused and disoriented as to place and often got lost in the ward. Her speech was incoherent, irrelevant, and showed marked delapidation of thoughts.

A course of deep-coma insulin treatment was started, which had to be discontinued because urticaria and angioneurotic edema developed. This allergic reaction to insulin also reappeared when zinc insulin was substituted for crystalline insulin. Treatment, therefore, was changed to electric shock therapy. The patient's condition became worse, and she started to complain of severe headaches. With this new symptom and a history of an old head injury, an electroencephalogram was made. The tracing showed abnormalities compatible with psychomotor epileptic discharge, idiopathic rather than of focal origin. Anticonvulsant therapy was recommended by the electroencephalographer, and on Nov. 1 treatment with phethenylate sodium, 2 grains (0.13 gm.) twice a day, was started. Soon after this treatment was instituted, definite improvement was observed in the patient's mental condition. The headaches subsided, and she seemed less confused. No routine blood cell counts were made during medication. The patient had received no other drugs since her admission to the hospital.

On Nov. 19, the 19th day of phethenylate therapy, the patient complained of being cold and aching all over. Her temperature was normal, and symptoms subsided spontaneously. On Nov. 21, she had a severe chill lasting over an hour, followed by a temperature of 105.4 F rectally. On Nov. 22, she felt comfortable except for vomiting after lunch. The maximal temperature on that day was 103 F.

On Nov. 23, the patient again had a chill, followed by a temperature of 104.8 F. At this time a medical consultation was requested. The patient had no symptoms, and she appeared cheerful and alert. Physical examination revealed a slight pallor of the skin but none of the mucous membranes. The throat was clear. There was a single area of ecchymosis of the conjunctiva of the right eye; otherwise the skin and mucous membranes were clear. No enlarged lymph nodes were palpable. The spleen was palpable on deep inspiration, but results of the rest of the physical findings were negative.

A roentgenogram of the chest was normal, and results of urinalysis and malaria smears were negative. A blood culture was taken and later reported sterile. A complete blood cell count showed 2,200 white blood cells with 51% neutrophils and a shift to the left. The red blood cell count, hemoglobin, and platelet count were normal. The diagnosis of granulocytopenia due to phethenylate sodium therapy was made.

Beginning Nov. 24, the patient was free of symptoms and felt well during the rest of the observation period, with the temperature remaining normal. Her subsequent course was characterized by changes in the blood cell count (see the accompanying table).

The total white cell count fell to its lowest level, 1,500, on Nov. 26 (the sixth day of illness), and granulocytes were completely absent in the peripheral count on Nov. 28 (eighth day). On that day a sternal puncture was done for a bone marrow study. The differential cell picture of the bone marrow showed a disturbance in maturation at the myelocyte level consistent with the diagnosis of granulocytopenia due to drug sensitivity. There was an increase in granulocytic myelocytes. The myeloid-erythroid ratio was found to be 1: 1.24. The megakaryocytes were normal and the platelets plentiful.

Neutrophils reappeared in the peripheral blood on Nov. 29 (9th day) and reached 50% in a 5,200 total white blood cell count on Dec. 4 (14th day). The peripheral red cell count did not show any abnormalities except for a transient 15% drop on the fifth and sixth days of illness. The platelet count remained normal throughout the entire period.

Phethenylate therapy was discontinued after the first blood cell count, Nov. 23 (third day), and treatment then consisted of the administration of procaine penicillin, 600,000 units once daily, and bed rest. In anticipation of pancytopenia, because of the red cell drop, blood transfusions were started on Nov. 25 and given for five consecutive days. Retrospectively, however, we do not believe that erythropoiesis was impaired in this case or that the transfusions played any role in the recovery of the patient.

Changes in the White Blood Cell Count in the Reported Case

Date (1951)	Day of Illness	White Blood Cell Count	Neutrophils, %	Lymphocytes, %
11/23	3	2,200	51	44
11/25	5	2,200	4	96
11/26	6	1,500	3	97
11/27	7	2,100	1	99
11/28	8	2,100	0	100
11/29	9	2,000	1	99
11/30	10	2,300	2	98
12/ 3	13	4,000	48	52
12/ 4	14	5,200	50	48

COMMENT

Apparently all the newer anticonvulsants are capable of depressing bone marrow in an occasional case. Only diphenylhydantoin sodium seems to be an exception to this. It is beyond the scope of this report to discuss in detail the control and prevention of the serious side-effects of the newer antiepileptic drugs, a topic comprehensively presented by others.[9] The advisability of frequent blood cell counts during the administration of the newer anticonvulsants, however, is emphasized.

SUMMARY

Agranulocytosis developed in a patient on the 20th day of administration of phethenylate ("thiantoin") sodium, 2 grains (0.13 gm.) twice a day. After cessation of treatment with the drug, the patient promptly recovered.

6. Gibbs, F. A., and Garvin, J., quoted by Best, W. R., and Paul, J. T.: Severe Hypoplastic Anemia Following Anticonvulsant Medication: Review of Literature and Report of a Case, Am. J. Med. 8: 124 (Jan.) 1950.

7. Best, W. R., and Paul, J. T.: Severe Hypoplastic Anemia Following Anticonvulsant Medication: Review of Literature and Report of a Case, Am. J. Med. 8: 124 (Jan.) 1950.

8. Weiss, H. A., and Hawley, W. D.: Pancytopenia Following the Use of Mesantoin and Thiantoin, U. S. Armed Forces M. J. 2: 83 (Jan.) 1951.

9. Abbott and Schwab.[2] Best and Paul.[7]

INTOXICATION DUE TO CHLORDANE

REPORT OF A CASE

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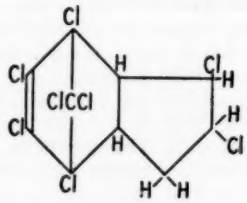
Chlordane is a commonly used insecticide with the empirical formula $C_{10}H_6Cl_8$ and the following structural formula.



Stohlman, Thorp, and Smith [1] have reported that it causes acute toxicity in rabbits equal to that caused by dichlorodiphenyltrichloroethane (DDT), a similar compound, in equivalent oral dosage ($L.D._{50}$), and that it causes greater chronic toxicity than does this similar compound because of greater cumulative action. Lehman [2] reported that toxicity in rats occurred after 12 weeks' administration of chlordane, 250 parts per million in the diet, the lowest intake causing gross demonstrable defects, whereas the toxic dose of dichlorodiphenyltrichloroethane was only 100 parts per million, but this required administration for 104 weeks. In dogs, administration of chlordane, 660 parts per million, caused death in four weeks; 2,640 parts per million of dichlorodiphenyltrichloroethane was necessary over a similar period. As with dichlorodiphenyltrichloroethane, continuous administration of chlordane to laboratory animals caused focal hepatic necrosis, edema, congestion and exudates in the lungs, and degenerative changes in intestinal submucosa and in the convoluted tubules of the kidneys. Organically bound chlorine was demonstrated in the urine of these animals. Bushland, Wells, and Radeleff [3] reported that, when chlordane was applied to cattle, hogs, sheep, and goats by spraying or in dips, signs of neurological and hepatic damage and subserosal hemorrhages resulted.

Statements by some investigators indicate the possibility of human intoxication from chlordane. Lehman [2] reported that the mean lethal dose of this compound in man is half that of dichlorodiphenyltrichloroethane and that smaller amounts than those of dichlorodiphenyltrichloroethane can be dangerous to man, in both divided and single doses. Hine [4] stated, "The halogenated hydrocarbons affect, in large amounts, the heart or central nervous systems, just as does chloroform; and in small amounts, if given over a period of time, produce liver and kidney damage, as does chloroform." On the other hand, Princi and Spurbeck,[5] in a study of 22 workers exposed to chlordane, aldrin, and dieldrin (compounds similar to chlordane) in the manufacture of these compounds, found no evidence of toxic effects as indicated by history, physical examinations, or laboratory tests. The men worked in atmospheres having up to 54 mg. of chlorinated hydrocarbons per cubic meter and were protected only by rubber gloves. Poisoning by swallowing an aldrin mixture has been reported by Spiotta.[6]

A review of the available medical literature has revealed no specific instance of chlordane causing toxic reactions in man. In the following case there was evidence of injury to the lungs, liver, and hematopoietic system after inhalation of chlordane.

REPORT OF A CASE

A 33-year-old Caucasian housewife was admitted to the United States Naval Hospital, San Diego, Calif., complaining of nausea, vomiting, and cough. She had been well until approximately one week previously, when a mildly acute infection of the upper respiratory tract had developed. Two or three days later, she entered her apartment at about 9:30 p. m. and noticed strong fumes of an insecticide, with which the apartment had been sprayed several hours earlier. She never opened her windows at night, fearing burglars, and she retired without airing the rooms. About 3 a. m. she awoke with severe cough and vomiting, and these symptoms continued unabated until admission four days later. The cough produced a moderate amount of thick, white sputum, which diminished in quantity. She did not complain of pain; nausea and vomiting were the only symptoms referable to the gastrointestinal tract. Past history was significant only in that, during an admission five months previously, after cerebral concussion, she had had an epileptiform seizure, the only one of her life; no abdominal organs were palpable at that time. She had returned from a prolonged stay at Guam 18 months prior to the last admission but had not been ill while there. She admitted occasional evenings of alcoholic intake of six or seven highballs but denied having had any alcohol for some time prior to the onset of this illness. The patient's private physician gave the information that she was a periodic "binge" drinker and that he was called to see her a few hours after she became ill by a woman friend of the patient, who was herself obviously intoxicated. He did not see or talk with the patient but suspected she also was intoxicated. She steadfastly denied this. It was ascertained that the insecticide used in the apartment was 1% or 2% chlordane, probably in an oil base similar to kerosene, used in an ordinary insect spray gun.

The patient was an alert, well-developed, slightly obese woman, appearing moderately ill and coughing frequently. Temperature, pulse, respiration, and blood pressure were normal. Physical findings were entirely within normal limits except for a smooth, firm, slightly tender liver edge, which descended three fingerbreadths below the right costal margin on inspiration. Breath sounds, voice sounds, and resonance were normal throughout both lungs, and no rales or rhonchi were heard. No telangiectasia and no lymphadenopathy were noted.

On admission the urine was normal. The Kahn reaction of the blood was negative, and the heterophil agglutination (not absorbed on guinea pig tissue) was positive in a titer of 1:14. Other admission laboratory findings are included in tables 1 and 2. The chest was within normal limits according to roentgenographic examination.

The opinions or assertions contained herein are the private ones of the writer and are not to be construed as official or reflecting the views of the Navy Department or the Naval Service at large.

1. Stohlman, E. F.; Thorp, W. T. S., and Smith, M. I.: Toxic Action of Chlordan, Arch. Indust. Hyg. **1**: 13 (Jan.) 1950.

2. Lehman, A. J.: Presented at Conference on Agricultural Chemicals, California Bureau of Adult Health, July 12, 1948.

3. Bushland, R. C.; Wells, R. W., and Radeleff, R. D.: Effect on Livestock of Sprays and Dips Containing New Chlorinated Insecticides, J. Econ. Entomol. **41**: 642, 1949; cited by Princi, F., and Spurbeck, G. H.: Study of Workers Exposed to the Insecticides Chlordan, Aldrin, Dieldrin, A. M. A. Arch. Indust. Hyg. **3**: 64 (Jan.) 1951.

4. Hine, C. H.: Presented at Conference on Agricultural Chemicals, California Bureau of Adult Health, July 12, 1948.

5. Princi and Spurbeck.[3]

6. Spiotta, E. J.: Aldrin Poisoning in Man: Report of Case, A. M. A. Arch. Indust. Hyg. **1**: 560 (Dec.) 1951.

The patient was afebrile throughout and showed rapid improvement. The cough was nonproductive on admission. Three days after admission the cough and emesis had practically ceased, and five days later the liver was no longer palpable. The only treatment was the administration of fluids parenterally on admission, hepatitis diet, and codeine for the cough. She was discharged 10 days after admission and was told to continue to have blood cell counts and liver function tests as an outpatient (tables 1 and 2). Unfortunately, blood drawn on Feb. 2, 1951, for a complete blood cell count clotted in the oxalate tube, and thereafter the patient failed to return to the hospital.

COMMENT

The pulmonary exudation exhibited by this patient and the hepatic dysfunction demonstrated by sulfobromophthalein retention and moderately positive cephalin flocculation are consistent with the toxic changes found to result from chlordane poisoning in animals. Hematologic reactions to dichlorodiphenyltrichloroethane have been reported,[7] including agranulocytosis from aerosol use, so that it is entirely possible that a similar compound, chlordane, caused a like reaction in this patient, with persistent depression of granulocytes, in one determination to 19%. The anemia was normocytic and hypochronic, and normal reticulocyte count and serum bilirubin concentration militate against hemolysis; the cause of the anemia is undetermined.

It might be argued that the blood picture and liver dysfunction were simply the result of cirrhosis in an alcoholic person in view of the slightly lowered albumin-globulin ratio (1.5:1), anemia, and leukopenia. However, the anemia was not macrocytic (mean cell volume, 94) as Tumen [8] stated is the tendency in cirrhosis, and the leukopenia was actually neutropenia. The serum albumin (3.8 gm.) per 100 cc. was only slightly lowered if at all (one source [9] quotes 3.5 to 5.6 gm. as normal, while others [10] give 4 gm. as the minimum normal value), and this is hardly valid evidence of cirrhosis. It should be noted also that hepatomegaly was not observed at the time of the patient's admission five months previously. Further, the liver enlargement found on this admission was no longer discernible after a few days and the degree of sulfobromophthalein retention diminished rapidly, indicating an acute process. Spider nevi and palmar flush were not seen.

TABLE 1.—*Hematological Findings*

	1/10/51	1/12/51	1/15/51	1/17/51	1/24/51
Hemoglobin, gm.	10.5	10.5	9.5	10.5	10.5
Red blood cells, millions	3.7	3.7	3.4 *	3.6	3.7
Hematocrit, %	....	....	32	34	....
Platelets	....	....	....	190,000	....
Reticulocytes, %	....	....	....	1.2	....
White blood cells	3,600	5,200	4,700	5,400	5,050
Basophils	....	....	1	....	1
Eosinophils	....	....	....	....	5
Segmented neutrophils	47	62	18	43	47
Lymphocytes †	53	38	80	57	47
Monocytes	....	....	1	....	....

* Mean cell volume, 94 cu. microns; mean corpuscular hemoglobin, 88 micromicrogram; mean corpuscular hemoglobin concentration, 30%.
† No abnormal lymphocytes reported.

In an editorial in THE JOURNAL [11] it was indicated that fat soluble chlorinated hydrocarbons, such as chlordane, are stored in adipose tissue and in the fat of all parenchymal cells, interfering with enzymatic processes in these cells. In view of this patient's obesity and the fact that she had definite alcoholic tendencies, it might be surmised that she had at least some increase in fat deposition in the liver, which could have made her more susceptible to hepatic insult.

It is unlikely that the abnormalities in this patient could have been caused by the solvent rather than by chlordane. The Council of Pharmacy and Chemistry of the American Medical Association in a report on dichlorodiphenyltrichloroethane [7] authorized the following statement: "The signs of solvent intoxication set in promptly, in contrast to the latent period of several hours required for the development of DDT symptoms." Approximately six hours intervened between the onset of the patient's exposure and development of cough and vomiting. It has also been stated [12] that xylene, kerosene, and other solvents may cause "irritation and other local symptoms, but are of minor importance when compared with the danger of system toxicity," referring particularly to the cutaneous absorption of aldrin and dieldrin, compounds similar to chlordane. It is possible that this patient's productive cough was due to bronchial irritation from the solvent fumes but hardly likely that such irritation would have caused a cough of over a week's duration. The hepatic and hematologic reactions could hardly have been due to solvent intoxication. Unfortunately, the patient was lost to observation before laboratory studies indicated a complete return to normal hepatic and hematopoietic functions.

TABLE 2.—*Results of Liver and Kidney Function Tests*

Test	1/10/51	1/15/51	1/19/51	1/24/51	2/2/51
Serum bilirubin	0.3	0.3	..	..	..
Sulfobromophthalein retention,* %	65	60	..	25	26
Cephalin flocculation					
24 hr.	2+	2+	0	..	1+
48 hr.	2+	2+	0	..	2+
Thymol					
Turbidity, units	1	1	1	..	0
Flocculation	0	0	0	..	0
Serum protein					
Albumin	..	..	3.8	..	..
Globulin	..	..	2.5 †	..	..
Phenolsulfonphthalein ‡					
15 min.	..	..	45%	..	..
60 min.	..	..	15%	..	..

* Dose of 5 mg./kg. of body weight, 45 minute interval.
† Ratio of 1.5:1.
‡ Intravenous injection.

SUMMARY

Toxic manifestations in an adult woman after inhalation of chlordane used in an insecticide spray are described. Involvement of lungs and liver consistent with

7. Pharmacologic and Toxicologic Aspects of DDT (Chlorophenothane U.S.P.), Report of the Council on Pharmacy and Chemistry, J. A. M. A. **145**: 728 (March 10) 1951.

8. Tumen, H. J.: Cirrhosis of the Liver, in Bockus, H. L.: Gastro-Enterology, Philadelphia, W. B. Saunders Company, 1946, vol. 3, p. 317.

9. Cantarow, A., and Trumper, M.: Clinical Biochemistry, ed. 4, Philadelphia, W. B. Saunders Company, 1949, p. 80.

10. Bing, J.; Naeser, J.; Rasch, G., and Røjel, K.: Serum Proteins in Normal People, Acta med. Scandinav. **126**: 351, 1946; cited by Hiller, G. I.; Huffman, E. R., and Levey, S.: Studies in Cirrhosis of the Liver: Relationship Between Plasma Volume, Plasma Protein Concentrations and Total Circulating Proteins, J. Clin. Investigation **28**: 322, 1949. Peters, J. F., and Eisenman, A. J.: Serum Proteins in Diseases Not Primarily Affecting Cardiovascular System or Kidneys, Am. J. M. Sc. **186**: 808, 1933.

11. Insecticide Storage in Adipose Tissue, editorial, J. A. M. A. **145**: 735 (March 10) 1951.

12. Aldrin and Dieldrin Poisoning, editorial, J. A. M. A. **146**: 378 (May 26) 1951.

chlordane intoxication demonstrated in animals and a hematologic reaction similar to that reported from dichlorodiphenyltrichloroethane exposure occurred The possibility of increased susceptibility in this patient to chlordane poisoning is discussed, as well as the possibility of other factors operating in the production of the symptoms and abnormal physical and laboratory findings.

Cherry and Kimbrough Sts. (Dr. Lemmon).

CUTANEOUS ALLERGY FROM LOCAL CONTACT WITH ISONICOTINIC ACID HYDRAZID

James W. Jordon, M.D., Buffalo

Isonicotinic acid hydrazid and its isopropyl derivative have recently been introduced for the treatment of tuberculosis. Because these drugs will find a widespread use, I believe the following report of a case of cutaneous sensitivity from local contact with isonicotinic acid hydrazid is of considerable interest. As far as I know, this is the first report of such a case.

REPORT OF A CASE

A white man, aged 34, a pharmaceutical chemist, was first seen on May 2, 1952, with the chief complaint of a skin eruption on his hands that had started on March 24, 1952. He stated that the only new product he had worked with prior to the onset of the eruption was isonicotinic acid hydrazid. He first worked with this drug on March 10, 1952. Because of the severity of the eruption he discontinued work from April 11 to April 21, and during this interval the rash had improved. On returning to work the eruption again became severe. When he was examined on May 2, 1952, he had an acute vesicular confluent dermatitis venenata involving the dorsal surface of both hands, the dorsal and ventral surface of both wrists, and to a slight extent the anterior aspects of the face and sides of the neck. He was asked to discontinue work because of the severity of the eruption and to bring in samples of the isonicotinic acid hydrazid as well as all other chemicals he had worked with prior to the onset of the dermatitis. He did this on May 20, and patch tests were made with the chemicals. At the end of 48 hours he showed a 4+ vesicular reaction to a tablet containing isonicotinic acid hydrazid. All other substances with which he was tested gave negative results. Because the tablet contained fillers and binders, he was asked to bring all the separate ingredients of the tablet for further patch test studies, and these were done on May 26, 1952. At the end of 48 hours he showed a vesicular reaction to the isonicotinic acid hydrazid, the other ingredients of the tablet giving negative results. Since discontinuing work and avoidance of contact with isonicotinic acid hydrazid, his dermatitis has gradually subsided. He was last seen on June 2, 1952, and was almost free of his eruption.

COMMENT

The development of the dermatitis venenata from local contact with isonicotinic acid hydrazid shows that this drug can induce epidermal sensitization if it contacts the skin. This means that in others who handle the drug, such as pharmacists, physicians, nurses, or patients, cutaneous sensitivity and dermatitis venenata may develop from local skin contact with it, and it should be suspected as a cause of unexplained dermatitis venenata in such persons.

71 North St. (2).

From the Department of Dermatology and Syphilology, University of Buffalo School of Medicine.

PLASTIC COMPRESSOR FOR ENUCLEATION AND EVISCERATION

Conrad Berens, M.D., New York

An "enucleation compressor" devised by Anthony,[1] was found to be most practical in controlling bleeding during enucleation and evisceration. The modification of the Anthony compressor herein described [2] is lighter and, because of the wicket shape, is easily manipulated. The instrument is made of lucite® (polymerized methyl methacrylate), with two arms bent at an angle of 45 degrees to the central grip. The central grip, which is 10 cm. long and 16 mm. in diameter, affords a comfortable hold. The arms of the plastic compressor are 9 cm. in length and taper in diameter from 16 mm. to 4 mm. The arms terminate in ovoid compressor tips, one 14 mm. and the other 11 mm. in diameter (fig. 1). The compressor is light in weight, inexpensive and may be sterilized in the usual manner for other plastic materials.

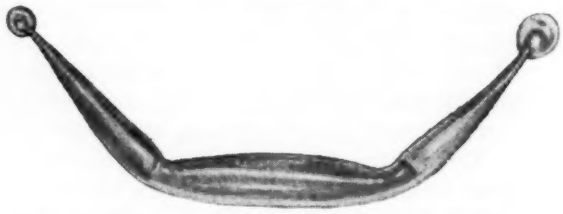


Fig. 1.—Plastic compressor for enucleation and evisceration.

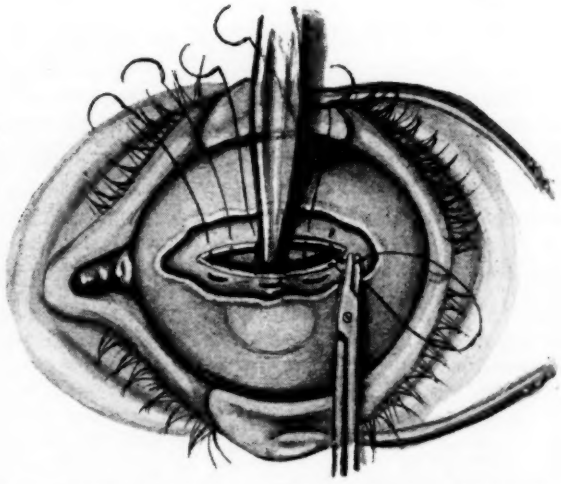


Fig. 2.—Compressor in scleral shell controls bleeding while sutures are being inserted.

The large ovoid compressor tip (for adults) or the smaller tip (for children) is introduced into Tenon's capsule immediately after the optic nerve is severed for enucleation or into the scleral shell after evisceration. Moderate constant pressure usually controls bleeding. The use of a compressor is more satisfactory for hematosis than is filling of the orbit or scleral shell with tampons and the use of digital pressure. Furthermore, with the use of tampons, the surgical procedure is necessarily halted

Aided by a grant from The Ophthalmological Foundation, Inc.

From the Department of Plastics, New York Eye and Ear Infirmary.

1. Anthony, D. H.: An Enucleation Compressor, Arch. Ophth. 18: 274 (Aug.) 1937.

2. The lucite® compressor described was made by R. O. Gulden, Philadelphia.

until the bleeding is stopped and the tampons removed from the orbit. In evisceration the scleral wound may be closed with the compressor in place (fig. 2), and the same is true of the suturing of Tenon's capsule in implantations following enucleation.

In several instances extrusion of an implant has been reported, which was apparently due to the fact that bleeding had not been adequately controlled before the implant was inserted. The compressor is of great assistance in controlling hemorrhage.

708 Park Ave.

COUNCIL ON PHARMACY AND CHEMISTRY

NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

R. T. STORMONT, M.D., *Secretary.*

Cortisone Acetate (See New and Nonofficial Remedies 1952, p. 322).

Merck & Company, Inc., Rahway, N. J.

Ophthalmic Ointment Cortone Acetate: 3.5 gm. tubes. An ointment containing 15 mg. of cortisone acetate in each gram.

Ophthalmic Suspension Cortone Acetate 0.5%: 5 cc. dropper bottles. An isotonic, buffered solution containing 5 mg. of cortisone acetate in each gram. Preserved with 0.02% benzalkonium chloride.

Ophthalmic Suspension Cortone Acetate 2.5%: 5 cc. dropper bottles. An isotonic, buffered solution containing 25 mg. of cortisone acetate in each gram. Preserved with 0.02% benzalkonium chloride.

Tablets Cortone Acetate: 5 mg.

Heparin Sodium-U. S. P. (See New and Nonofficial Remedies 1952, p. 208).

Abbott Laboratories, North Chicago, Ill.

Solution Heparin Sodium: 10 cc. vials. A solution containing 5,000 U. S. P. units of heparin sodium in each cubic centimeter; 5 cc. vials. A solution containing 10,000 U. S. P. units of heparin sodium in each cubic centimeter. Preserved with 0.18% methylparaben and 0.02% propylparaben.

Aminophylline-U. S. P. (See New and Nonofficial Remedies 1952, p. 294).

The Bowman Bros. Drug Company, Canton, Ohio.

Tablets Aminophylline: 0.1 gm. plain and 0.2 gm. enteric coated.

Aureomycin Hydrochloride-U. S. P. (See New and Nonofficial Remedies 1952, p. 117).

Lederle Laboratories Division, American Cyanamid Company, Pearl River, N. Y.

Capsules Aureomycin Hydrochloride: 100 mg.

Methamphetamine Hydrochloride-U. S. P. (See New and Nonofficial Remedies 1952, p. 185).

Rexall Drug Company, Los Angeles.

Tablets Methamphetamine Hydrochloride: 2.5 mg. and 5 mg.

COUNCIL ON FOODS AND NUTRITION

Owing to the current interest in sodium-restricted diets, the Council on Foods and Nutrition has authorized the publication of the following article.

JAMES R. WILSON, M.D., *Secretary.*

NUTRITIONAL IMPLICATIONS OF SODIUM RESTRICTION

In the preparation of diets restricted to less than 0.5 gm. of sodium daily, alterations from the diet usually considered optimum may be necessary. Thus, a reduction in animal protein and the nutrients usually associated with it may be required and certain other foods specifically prepared to remove naturally occurring sodium may be added to the diet. These alterations in the usual dietary customs of persons may sometimes compromise optimum nutrition, a matter to be seriously considered by physicians prescribing a low-sodium diet.

Such changes in the diet as the omission of salt for seasoning, using sweet butter, low-sodium bread, and omitting foods naturally high in sodium should involve no nutritional difficulties, except for any attendant decrease in taste appeal. The same is also true for processed foods packed without added sodium salts.

Limitations in the amount of meat and eggs allowed per day will sometimes be necessary, particularly if the daily sodium intake is to be 200 mg. or less. This involves a decrease in protein of high biological value and of the concomitant vitamins of the B complex.

The processing of foods to remove natural sodium may decrease the content of certain other nutrients. Products such as these are appearing on the market in increasing numbers and may be highly desirable because of the low levels of sodium they provide. At present, the extent of the reduction in nutrients other than sodium in these foods is not known, in many instances, but efforts will be made to procure this information and make it available to physicians.

Thus, the physician prescribing a low-sodium diet must weigh carefully the therapeutic benefits to be expected against the consequences of a possible reduction in the intake of essential nutrients. This may be particularly true of persons already malnourished or with conditioning factors such as defects in digestion and absorption or abnormalities in intermediary metabolism.

The Council will consider for acceptance foods packed or prepared without added sodium provided the food is otherwise acceptable and provided the sodium content appears on the label (in milligrams per 100 gm.) in addition to a statement such as "Packed without added sodium." The Council will also consider foods processed to remove naturally occurring sodium. When significant loss of nutrients, other than sodium, is shown to have occurred, a statement to this effect must also appear on the label and detailed information concerning this reduction in specific nutrients must be made available to the Council and to physicians likely to use the product.

ACCEPTED FOODS

The following product has been accepted as conforming to the rules of the Council.

JAMES R. WILSON, M.D., *Secretary.*

B. M. Mishler Company, Pasadena, California.

Bradford Brand Dietetic Pack Tuna. Ingredients: Light meat tuna and distilled water.

Analysis (submitted by distributor).—Total solids 30.6%, moisture 69.4%, protein (N × 6.25) 28.3%, fat (ether extract) 0.75%, carbohydrates (by difference) 0.15%, sodium 40 mg./100 gm., cholesterol 70 mg./100 gm.

Calories.—1.22 per gram; 35 per ounce.

Use.—A useful adjunct for the planning of low fat, low sodium dietaries.

THE JOURNAL
OF THE AMERICAN MEDICAL ASSOCIATION
535 N. DEARBORN ST. . . . . CHICAGO 10, ILL.
Edited by . . . . . AUSTIN SMITH, M.D.
Associate Editor . . . . . JOHNSON F. HAMMOND, M.D.
Editor for Medical Literature Abstracts . GEORGE HALPERIN, M.D.

Subscription price . . Fifteen dollars per annum in advance
Cable Address . . . . . "Medic, Chicago"

PREVENTION OF RABIES

The physician who treats a patient exposed to the bite or saliva of an animal is confronted now with a more difficult problem than in the past. Current developments in the field of rabies prophylaxis have led to conflicting opinions concerning the indications for the Pasteur treatment, the degree of efficacy of this form of treatment, and the incidence of postvaccinal neurological sequelae. In December, 1951, Koprowski and Cox [1] noted in a review that until recent years it was customary to give the Pasteur treatment to all persons exposed to the saliva of an animal that behaved abnormally. There has been a trend, however, toward greater conservatism in using the Pasteur treatment. Behind this change in attitude lie two major factors: the questionable value of the Pasteur treatment in cases in which severe wounds have been inflicted by obviously rabid animals, and the occurrence of a significant number of serious postvaccinal neurological sequelae.

Pait and Pearson,[2] using data collected in the county of Los Angeles for 1940 to 1946, report an incidence of neuroparalytic reactions of 1:600 among persons receiving Semple vaccine, while the chances of acquiring rabies following a known dog bite in the city of Los Angeles varied from 1:1400 to 1:2100. Similarly, in Manhattan among 3,305 patients who received the Pasteur treatment during the period 1946 to 1949, in 6 postvaccinal paralysis developed, an incidence of 1:551.[3] On the other hand, Sellers [4] found 7 cases of post-treatment paralysis among about 50,000 patients treated, an incidence of 1:7000. The exact incidence of these postvaccinal reactions is not known, but a significant number of neuroparalytic sequelae, including some fatalities, do occur. Thus in deciding whether to administer antirabies vaccine the physician must balance the risk of a potential serious postvaccinal reaction against the possibility of the development of rabies.

Indications for vaccine treatment in cases of animal bites were considered by the first session of the WHO Expert Committee on Rabies, held in April, 1950. The committee published [5] detailed indications for the use of vaccine treatment that are designed to avoid, as much as possible, indiscriminate use of the Pasteur treatment. Use of the Pasteur treatment was favored only in cases of bites and licks of uncaptured, wild, or rabid animals and in cases of multiple bites of the head, neck, and shoulders. Similar conservatism has been advocated by Sellers,[6] who considers antirabic treatment contraindicated in the following circumstances: (1) when there is no broken skin anywhere on the body, including face or mouth; (2) if previous wounds are known to be over 24 hours old or are covered with an unbroken scab; (3) if the tooth wounds were made through untorn clothing (such wounds are usually bruises); (4) if exposure is limited to handling only the dog or objects contaminated with the saliva, or to drinking the milk of rabid cows or goats; (5) if the wounds were inflicted not less than seven days prior to the detection of visible signs of the disease; and (6) if the animal remains normal for as long as seven days after inflicting the wounds. Reimmunization should be avoided for borderline exposure regardless of the time elapsed since the last treatment, according to Sellers. He recommends that re-treatment be limited in any case to a short booster series of five or six injections.

The use of antirabies serum, although known since 1889, has never gained prominence; however, since 1948, concentrates of antirabies serum prepared in sheep or rabbits have been available for clinical trial in the United States. The series of human patients treated with antirabies serum is not yet sufficiently large to draw definite conclusions, but Koprowski reports that no person who has received antiserum has died of rabies.[1] At the time of Koprowski's report,[1] in December, 1951, antiserum had been given to 48 persons. Of these, 29 were bitten by animals shown to be rabid. He recommended the administration of the serum as soon as possible after exposure, preferably within 24 hours. He used it in conjunction with vaccine, which may be administered 24 hours after administration of the antiserum, or possibly somewhat later, since rabies antibodies remain present for 7 to 10 days after passive immunization. Serum sickness was noted in about 20% of those treated with rabbit serum and in a much larger number of those treated with sheep serum. Therefore, the production of serum in sheep has been discontinued in favor of horse or rabbit serum. Although the usual precautions to be observed with the use of serums apply here, serum sickness would be less serious than rabies or a serious neuroparalytic complication. Antiserum is particularly suited for therapy of those patients with severe bites of the head or neck in which the Pasteur treatment has been least efficacious. If further clinical studies confirm the successful results obtained in experimental work [7] with the use of antiserum, it may be possible to reduce the number of injections of phenolized vaccine when antiserum is used adjunctively.[1] It should thus be possible to reduce the incidence of neurological sequelae, since it is known that paralytic complications occur more frequently when an increased number of injections of vaccine are given.

A recent departure from the presently used phenolized antirabies vaccine is the development of the chick-

1. Koprowski, H., and Cox, H. R.: Recent Developments in the Prophylaxis of Rabies, Am. J. Pub. Health **41**: 1483-1489 (Dec.) 1951.
2. Pait, C. F., and Pearson, H. E.: Rabies Vaccine Encephalomyelitis in Relation of the Incidence of Animal Rabies in Los Angeles, Am. J. Pub. Health **39**: 875-877 (July) 1949.
3. Koprowski, H., and Le Bell, I.: The Presence of Complement-Fixing Antibodies Against Brain Tissue in Sera of Persons Who Had Received Antirabies Vaccine Treatment, Am. J. Hyg. **51**: 292-299 (May) 1950.
4. Sellers, T. F.: Complications of Antirabic Treatment, J. M. A. Georgia **36**: 30-35 (Jan.) 1947.
5. Expert Committee on Rabies: Report on the First Session, World Health Organization Technical Report Series, 3-17 (Nov.) 1950.

embryo-adapted Flury strain of live rabies virus vaccine.[8] This vaccine has been used widely and with apparent effectiveness in the immunization of dogs and gives promise of eliminating the postvaccinal neuroparalytic sequelae, which are thought by most investigators to be due to sensitization to brain tissue. A recent communication [9] from Israel reports that since the start of the antirabies campaign in October, 1950, carried on with the assistance of WHO, the number of rabies cases in animals has dropped from an average of 100 a year, before the start of the campaign, to 10 in the 15 months prior to the report. This program includes a mass vaccination of dogs with egg-adapted vaccine (Flury strain). There were no deaths in humans from rabies in Israel in 1951, whereas there were 20 such deaths between 1948 and 1950. Although it is too early to determine to what extent vaccine has brought about the decline in rabies incidence, it is believed that the mass vaccination has played an important part. The egg-adapted vaccine has proved harmless to dogs and seems to give a greater and longer immunity than other vaccines, according to this communication. This vaccine has also been administered to about 50 persons without undue reactions resulting.[10] It appears to offer possibilities for use in humans but further study of the problem is required.

The ultimate solution to the problem of rabies in human beings is complete eradication of the disease in animals. It has been demonstrated that the disease may be controlled by mass vaccination in dogs and thus prevented in human beings when dogs are the sole source of infection. In view of the widespread geographic distribution of rabies and the many species of animals involved, however, complete eradication in animals is extremely difficult. Therefore, continued research to improve agents for prevention of this disease in exposed persons is indicated. Current developments in rabies prophylaxis, although they do not yet offer a final solution to the problem of rabies prevention, seem to justify an optimistic outlook for the future.

WHY MEDICAL GROUPS DISSOLVE

The Bureau of Medical Economic Research has recently published Bulletin 90, "Discontinuance of Medical Groups, 1940-1949." [1] Of the 441 medical groups in existence at the start of the 1940's, 82 were discontinued during the decade; of these 82, 40 were dissolved entirely, 27 were still in existence but had ceased to meet the requirements of the Bureau's definition of a group, and 15 were reorganized. By restricting their study to the groups that were discontinued and to the reasons therefor, the authors have avoided any discussion of the pros and cons of group practice, particularly from the standpoint of the patient. They have taken a leaf out of research publications in the field of marketing and have tried to set forth the reasons why some groups fall by the wayside, in the hope that such an analysis will be helpful to a physician who is contemplating organizing, joining, or reorganizing a medical group or choosing individual or nongroup partnership practice.

GRANTS BY NATIONAL FUND FOR MEDICAL EDUCATION PAST $2,500,000 MARK

With the awarding of its third series of grants to the medical schools this month, the National Fund for Medical Education has passed the $2,500,000 mark in the funds distributed to the medical schools in the past 12 months.

Included in this total is the $1,417,752 that has been raised by the American Medical Education Foundation to date. The important contributions of the medical profession to this nationwide program to raise funds for medical education has been formally recognized by the National Fund for Medical Education by the following resolution adopted unanimously by the Trustees of the fund at their last meeting.

"The Board of Trustees extend a vote of appreciation to the American Medical Association and the American Medical Education Foundation for the fine progress that they have made, and for their cooperation in turning over their collections to the Fund for distribution by it to the medical schools."

It is thus clear that the medical profession is setting an example of self-help that should stimulate industry and other groups in American society to make their contributions to this important undertaking.

The American Medical Education Foundation has set an annual goal of 2 million dollars to be raised by the medical profession. It is hoped that this goal can be reached for the first time during 1952. Prospects are reasonably good that this can be accomplished. Already 3,255 individual contributions have been received, which is 42.3% more than the total number of contributions received during the entire year 1951. Several state societies are just getting their campaigns into full operation. The Woman's Auxiliary, which has made two handsome contributions from its own funds, is embarking on an active campaign to: (1) stimulate gifts from individual physicians, (2) seek the financial support of over 1,000 auxiliaries, and (3) carry on a vigorous public education program on behalf of the Foundation.

When the medical profession achieves its goal of $2,000,000 annually the National Fund will be well on the way to its goal of raising $5,000,000 in unrestricted funds each year. When this has been accomplished, the more acute financial threats to the stability and continuing high quality of the medical schools should be substantially relieved. Physicians who have not yet contributed to the American Medical Education Foundation are urged to make their contributions promptly either through their state organizations or directly to the Foundation at 535 N. Dearborn Street, Chicago 10.

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6. Cautions Care in Antirabic Vaccine Use, Selected Reports, Pub. Health Rep. **66**: 1117-1118 (Aug. 31) 1951.

7. Koprowski, H.: Experimental Studies on Rabies Virus, Canad. J. Pub. Health **40**: 60-67 (Feb.) 1949.

8. Koprowski, H., and Cox, H. R.: Studies on Chick Embryo Adapted Rabies Virus: Culture Characteristics and Pathogenicity, J. Immunol. **60**: 533-554 (Dec.) 1948.

9. Rabies Campaign, Foreign Letters, J. A. M. A. **149**: 1153 (July 19) 1952.

10. Starr, L. E.: What the Physician Should Know About Rabies, South. M. J. **45**: 370-374 (April) 1952.

1. Dickinson, F. G., and Bradley, C. E.: Discontinuance of Medical Groups, 1940-1949, Chicago, Bureau of Medical Economic Research, American Medical Association, 1952. A copy of Bulletin 90 may be obtained by writing to the Bureau, 535 North Dearborn Street, Chicago 10.

MEDICAL NEWS

CALIFORNIA

Discussion of the Normal Child.—The Southern California Society for Mental Hygiene on July 15 held a discussion at the Institute of Aeronautical Sciences in Los Angeles on guides to understanding the growth and development of the normal child. In addition to a community panel, the following physicians participated: Reynold A. Jensen, Minneapolis; Martha G. MacDonald, Palo Alto; C. Morley Sellery, Los Angeles; and Hale F. Shirley and Emmy Sylvester, San Francisco. Dr. Nathan K. Rickles of Beverly Hills, neuropsychiatric consultant, VA Hospital at Sawtelle, was moderator.

Personals.—Dr. Robert Wartenberg, clinical professor of neurology, University of California School of Medicine, San Francisco, has been elected an honorary member of the Italian Neurological Society.——Dr. John H. Aldes, Los Angeles, presented a paper entitled "The Use of Ultrasonic Therapy in the Treatment of Hypertrophic Arthritis with and Without Radiculitus—Geriatric Group" at the International Congress of Physical Medicine in London, England, July 14-19. He also attended the orthopedic association's meeting in London and planned to tour the rehabilitation centers in the Scandinavian countries before returning to the United States.

COLORADO

New Research Head at National Jewish Hospital.—Dr. Gardner Middlebrook, associate in the department of pathology and microbiology at the Rockefeller Institute for Medical Research in New York, has been appointed director of research and laboratories at the National Jewish Hospital in Denver to succeed Dr. Harry J. Corper, who has retired after 32 years of service as the institution's research head. The National Jewish Hospital, opened in 1899, is a nonsectarian tuberculosis center.

CONNECTICUT

Cerebral Palsy Study.—The cerebral palsy study conducted by the Connecticut State Department of Health in 1950 included determinations of the prevalence; the medical, social, psychological, and educational aspects; and the medical, educational, and institutional needs of cerebral palsy patients less than 21 years of age. The rates for children 5 to 9 and 10 to 14 years of age were much higher than for younger and older children. These differences in rates were considered to have been due to poor reporting or recognition of patients among infants and to the eventual adjustment to the diseases, favorable or unfavorable, among older persons. Specific needs of cerebral palsy patients were determined by detailed studies of sample groups of 130 Connecticut children. Less than half the Connecticut patients (34.3%) were considered as having potentialities for improving on an ambulatory system of therapy, and 51.7% of the children were recommended for inpatient care.

DISTRICT OF COLUMBIA

Freedmen's Hospital Interns and Residents.—At the annual session of the Association of Former Internes and Residents of Freedmen's Hospital, Dr. R. Frank Jones, professor of urology at Howard University College of Medicine, was elected president; Dr. Peyton R. Higginbotham, Bluefield, W. Va., president-elect; Dr. Charles R. Chephas, New Brighton, Pa., secretary; and Dr. L. Greeley Brown, Elizabeth, N. J., treasurer. The 31st session will be a memorial to Dr. William A. Warfield Sr., who was surgeon-in-chief of the hospital for 35 years.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education and public health. Programs should be received at least three weeks before the date of meeting.

ILLINOIS

Test for Insecticide Poisoning.—Testing of blood specimens for the detection of poison from exposure to insecticides is now offered by the diagnostic laboratories of the State Department of Public Health. This new service is made possible by the development in the department's laboratories of a specially prepared heparinized tube for collecting the blood samples. The special tubes may be had on request by physicians who need them for immediate use. Requests should be addressed to Howard J. Shaughnessy, Ph.D., Deputy Director in Charge of Laboratories, 1800 W. Fillmore St., Chicago 12.

The new test is for detection of poisoning with organic phosphates. As poisoning from such phosphates is cumulative, the test may be used best as a preventive, but it is helpful also in confirmation of diagnosis.

Chicago

Gift for Polio Research.—A check for $7,350 to further polio research was presented recently to Michael Reese Hospital by the Merton Davis Memorial Fund. This brings the total contributions of the Merton Davis Memorial Club to $24,450. This club was organized three years ago by a group of high school students in memory of a classmate who died of polio.

Dr. Frank Goes to North Carolina.—Dr. Edward Colman Frank has been appointed associate professor of psychiatry at the University of North Carolina School of Medicine, Chapel Hill, and will assume his new duties Sept. 1. Dr. Frank, who is adjunct psychiatrist at the Psychosomatic Institute of Michael Reese Hospital, is also consultant to Portal House Outpatient Clinic, Chicago; the Family Service Organization, Louisville, Ky.; and the alcoholic unit of the mental health centers of the state of Illinois. Dr. Frank was formerly psychiatrist for the David B. Rotman Research Laboratory of the Psychiatric Institute of the Municipal Court of Chicago.

Dr. Soskin Resigns as Director of Research Institute.—Dr. Samuel Soskin will resign as director of the Medical Research Institute of Michael Reese Hospital and dean of the hospital's postgraduate school, Sept. 1, to enter private practice in his specialty (diabetes and other metabolic and endocrine disorders) in Los Angeles. Dr. Soskin has been a full-time staff member of the hospital since 1929, when he was appointed director of metabolic and endocrine research, and from 1943 to 1950 he served as medical director of the institution. For 20 years he served first as assistant professor and later as professorial lecturer in physiology at the University of Chicago. Recently he has been an associate professor of medicine at Northwestern University Medical School. Dr. Soskin is a past president of the Chicago Society of Internal Medicine and of the Chicago Diabetes Association and a former chairman of the Illinois section of the Society for Experimental Biology and Medicine. He will continue as editor-in-chief of *Metabolism*, a scientific journal, and will devote time to research, teaching, and private practice.

INDIANA

Hospital Fund Drive.—Dr. Lawson J. Clark, Indianapolis, heads a 16 physician committee, which will serve among the physicians for the $12 million hospital fund drive. Pledges will be sought on a five year basis. The Hospital Development Association has already received in pledges a total of $1,400,000.

Anniversary of Medical Foundation.—An invitational open house followed by a dinner marked the 40th anniversary of the South Bend Medical Foundation, Inc. Dr. Alfred S. Giordano has been director of the foundation since 1922. Dr. Robert A. Moore, professor of pathology and dean of the school of medicine, Washington University School of Medicine, St. Louis, addressed the guests.

NEW YORK

Dr. Simpson Honored.—Dr. Leo F. Simpson of Rochester was recently awarded an honorary degree of doctor of science by St. Bonaventure University as "an outstanding physician and surgeon who has won the universal admiration of colleagues, assistants, patients and the public." Dr. Simpson is a past president of the Monroe County Medical Society, the Rochester Academy of Medicine, and the Medical Society of the State of New York.

New York City

Society News.—The New York Roentgen Society announces election of the following officers: Dr. John L. Olpp, Tenafly, N. J., president; Dr. Irving Schwartz, vice-president; Dr. Harold W. Jacox, secretary; and Dr. Jacob R. Freid, treasurer.

Personals.—Dr. Norman H. Joliffe, director of the Bureau of Nutrition of the New York City Department of Health, was recently elected president of the National Vitamin Foundation, Inc., an industry-supported institution for financing research in nutritional fields.——Dr. H. Houston Merritt, professor of neurology at Columbia University College of Physicians and Surgeons, has been appointed to the advisory committee on virus research and epidemiology of the National Foundation for Infantile Paralysis.

Palsy Center Affiliates with Medical College.—Nassau County's new $500,000 Cerebral Palsy Diagnostic and Treatment Center, recently completed at Roosevelt, L. I., has become affiliated with New York Medical College, Flower-Fifth Avenue Hospitals. The affiliation will make available to the center the services of specialists and at the same time will provide training for medical students and physicians. Dr. Milton J. Wilson, professor of orthopedics, Dr. Lawrence B. Slobody, professor of pediatrics, and Dr. Robert V. Martin, director of the new center, will act with Dr. J. A. Werner Hetrick as an advisory committee. The new center, built through public contributions and with the assistance of local trade unions, which donated thousands of free man-hours of labor, went into full operation July 1. At capacity, it will provide outpatient treatment for 295 children with palsy at a time.

NORTH CAROLINA

Dr. Warren Joins Duke Faculty.—Dr. James V. Warren, president of the American Federation for Clinical Research, has been appointed professor of medicine at The Duke University School of Medicine, Durham. Formerly a professor of medicine and physiology at Emory University School of Medicine, Atlanta, Dr. Warren recently received a grant-in-aid from the American Heart Association for research in heart and blood diseases at Duke. In addition to his duties at Duke, he will help enlarge the medical department of the new Veterans Administration Hospital in Durham. Dr. Warren recently was given a brief leave of absence to serve on a U. S. Navy medical project in Africa.

OHIO

Research in Leukemia.—A foundation to support research in leukemia has been established at Ohio State University College of Medicine through a gift of $18,946 by Dr. and Mrs. James O. Beavis of Dayton, whose son, James Ewing Beavis, was a victim of the disease last summer.

Course in Heart Disease of Children.—A course in heart disease of children will be offered at the Cincinnati Children's Hospital and allied institutions Sept. 16-19. There will be opportunities for examination of patients and observation of new techniques of diagnosis. The course will be restricted to 10 physicians. A fee of $50 will be charged. For information, address the Children's Heart Association, 3231 Burnet Ave. (General Hospital), Cincinnati 29.

State Society Encourages Rural Practice.—The committee on rural health of the Ohio State Medical Association recently inaugurated a series of informal lectures to encourage senior medical students to take up the general practice of medicine as a career. The series of lectures was the culmination of several years of effort on the part of the committee to bring forth practical talks that would present the facts on rural medical practice. Topics covered in the series included: "Selecting the Place to Practice"; "Type of Practice Encountered"; "Hospital Connections and Emergencies"; "The Economics of a Rural Practice"; and "The Physician and His Community." Dr. J. Martin Byers, Greenfield, chairman of the committee on rural health, and Dr. Edmond K. Yantes, Wilmington, a member of that committee and of the Committee on Medical Service Plans of the Association, served as volunteer lecturers. The committee will meet during the summer to plan with the Ohio State University medical faculty the program for next year. The possibilities of making similar arrangements with both of the other medical schools in the state will be explored.

WEST VIRGINIA

Dr. Kemper Retires as Health Officer.—Dr. Americus Kemper of Clarksburg retired July 1 as health officer for Harrison County after 21 years of service. On the day before his retirement, the staffs of the Harrison County Health Department and the Harrison tuberculosis office, and the school nurse presented him with a camera, and the Harrison County Medical Society gave him a gold watch at a banquet.

Personals.—Dr. David C. Prickett of Weston, health officer for district no. 4, has accepted appointment as director of the Marion County Health Department to succeed Dr. A. Glenn Evans, resigned.——Dr. Benjamin M. Drake of Charleston, deputy state director of health, has resigned to accept appointment as head of the division of preventive medical services of the Kentucky State Department of Health with headquarters in Louisville.——Dr. Frank J. Holroyd of Princeton, past president of the West Virginia State Medical Association, has been reappointed by Governor Patteson as a member of the medical licensing board for the term ending June 30, 1957.——Dr. Hu C. Myers of Philippi has been reappointed by Governor Patteson as a member of the advisory board of the hospital licensing program of the State Department of Health. His term will expire June 30, 1959.

GENERAL

Group Psychotherapy Seminars.—The Group Psychotherapy Institute, New York, has announced the addition of three seminars for the 1952-53 academic year, each to run for 30 consecutive two-hour sessions beginning October, 1952: (1) "Survey Seminar in Group Psychotherapy," (2) "Activity Group Therapy with Children," and (3) "Analytic Group Psychotherapy." Among the instructors will be Drs. Nathan W. Ackerman, Aaron Stein, James J. Thorpe, Joseph J. Geller, and Hyman Spotnitz, New York, and Samuel B. Hadden, Philadelphia. Information may be obtained from the Institute, 105 E. 22nd St., New York 10.

Research Fellowships.—The American College of Physicians announces that a limited number of fellowships in medicine, carrying a stipend of $3,000-$3,500, will be available from July 1, 1953 to June 30, 1954. The fellowships are designed to provide an opportunity for research training in the basic medical sciences or in the application of these sciences to clinical investigation. Assurance must be provided that the applicant will be acceptable in the laboratory or clinic of his choice and that he will be provided with the facilities necessary for the proper pursuit of his work. Application forms, supplied on request to the American College of Physicians, 4200 Pine St., Philadelphia 4, must be submitted in duplicate not later than Oct. 1.

Applications for Grants in Cancer Research.—The Committee on Growth of the National Research Council, acting for the American Cancer Society, is accepting applications for grants in support of cancer research. Applications for new grants received before Oct. 1 will be considered during the winter, and grants recommended at that time will become effective July 1, 1953. Investigators now receiving support will be notified individually regarding application for renewal of these grants. The research program includes, in addition to clinical investigations on cancer, fundamental studies in the fields of cellular physiology, morphogenesis, genetics, virology, biochemistry, metabolism, nutrition, cytochemistry, physics, radiobiology, chemotherapy, endocrinology, and environmental cancer. During the past year the American Cancer Society, on recommendation of the Committee on

Growth, has awarded approximately 250 grants totaling about $1,700,000. Application blanks may be obtained from the Executive Secretary, Committee on Growth, National Research Council, 2101 Constitution Ave., Washington 25, D. C.

Rocky Mountain Radiological Society Conference.—The annual Mid-Summer Conference of the Rocky Mountain Radiological Society will be held in Denver at the Shirley-Savoy Hotel Aug. 7-9. Dr. Philip J. Hodes, Philadelphia, will discuss the roentgen manifestations of (1) pancreatic and periampullary disease and (2) cerebellopontine angle tumors; Dr. Harold O. Peterson, St. Paul, will speak on the roentgen diagnosis of benign gastric ulcer and unusual neurological conditions with diagnostic roentgen findings; Dr. George H. Ramsey, Rochester, N. Y., will present cinefluorographic analysis of (1) some movements of the cervical spine and (2) the causes of dysphagia; and Dr. A. Justin Williams, San Francisco, will speak on the roentgen diagnosis of intra-abdominal hernia.

A symposium on diseases of animals transmissible to man will be presented. Evening meetings will include a joint session with the Denver Medical Society, followed by Dutch lunch, and an informal banquet. The annual picnic on Saturday afternoon will conclude the conference.

National Medical Association.—The National Medical Association, Inc., will meet in Chicago, Aug. 11-15, under the presidency of Dr. Joseph G. Gathings of Washington, D. C. Headquarters of the meeting will be at the DuSable High School, Wabash Ave. and 50th St. On Monday morning there will be a panel discussion on "The President's Committee on the Health Needs of the Nation." Tuesday afternoon "Late Syphilis" will be presented as a symposium and illustrated lecture. The Wednesday morning session will open with the annual Stubbs Lecture on "Interesting Lesions of the Gastrointestinal Tract" by Dr. Ellsworth E. Hasbrouck, Chicago. On Wednesday afternoon there will be symposiums on modern obstetrical procedures and leukorrhea. A symposium on gastritis will be held Thursday afternoon, and on Friday time will be given to psychiatric problems that confront the general practitioner. Another symposium, to be held at the same time, will deal with common fractures of the upper and lower extremities.

Photography in Medicine and Biology.—How to make photography serve more effectively in medicine and biology is the subject of a symposium at the Hotel New Yorker, New York. Aug. 12 as part of the convention of the Photographic Society of America. Among many others, Dr. David S. Ruhe of New York, director of the Audio-Visual Institute of the Association of American Medical Colleges, will speak on "The Changing Ideology of Medical Teaching Motion Pictures."

Techniques and equipment for the types of photography carried on in a general hospital will be described by Leonard A. Julin, of the Mayo Clinic, Rochester, Minn. Dr. Dan H. Gordon, professor of ophthalmologic surgery at Cornell University Medical College, will review the rapid advances in techniques for photographing the eye. Co-chairmen of the symposium are Dr. Milton G. Bohrod of Rochester, N. Y., General Hospital, and H. Lou Gibson of the Medical Division of Eastman Kodak Company. Registration fee for the day is $2. The Photographic Society of America has headquarters at 2005 Walnut St., Philadelphia 3.

Physical Medicine Congress.—The annual scientific session and instruction seminar of the American Congress of Physical Medicine will be held Aug. 25-29 at the Roosevelt Hotel, New York, under the presidency of Dr. Robert L. Bennett of Warm Springs, Ga. Lecturers for the instruction seminar include: Drs. Charles O. Bechtol, San Francisco; Robert L. Bennett, Warm Springs, Ga.; Frances A. Hellebrandt and Meyer A. Perlstein, Chicago; Frank H. Krusen, Rochester, Minn.; Allen S. Russek and Joseph D. Sullivan, New York; and Malford W. Thewlis, Wakefield, R. I. The charge for the eight lectures is $15.

On Monday there will be a luncheon of the Advisory Committee on Education, Council on Physical Medicine and Rehabilitation, American Medical Association. This will be followed by an educational conference, at which the following topics will be discussed: "University Sponsored Graduate Fellowship Training in the Medical Specialties," "Method of AMA Residency Approval," "Undergraduate Instruction in Physical Medicine and Rehabilitation," and "Report of the Advisory Committee of the Council on Physical Medicine and Rehabilitation of the American Medical Association." On Wednesday Dr. Frank H. Krusen, professor of physical medicine and rehabilitation, Mayo Foundation, will deliver the second John Stanley Coulter Memorial Lecture on "Report on the International Congress of Physical Medicine." Wednesday evening the annual congress dinner will be held.

On Thursday at 10 a. m. there will be a rehabilitation symposium, with the following presentations:

Howard A. Carter, M.E., Chicago, Rehabilitation of the Hard of Hearing.

Samuel S. Sverdlik, New York, Evaluation of Speech Training in the Rehabilitation of the Aphasic.

Everill W. Fowlks, Portland, Ore., Patient Evaluation by Wechsler Bellevue Test.

Charles H. Reagan, Tuscaloosa, Ala., Rehabilitation of 120 Lobotomized Patients in a VA Hospital.

Edith L. Kristeller, New York, Work Program for the Disabled Housewife.

Marion Strauss Lesser, M.A., and Robert C. Darling, New York, Some Follow-Up Studies in Rehabilitation at the Institute for the Crippled and Disabled.

Adam Peylan, Tel-Aviv, Israel, Combined Use of Hydrotherapy and Sweating Cure in Certain Arthritis Problems.

Heart Association Seeks Research Applicants.—New research applications in cardiovascular and related fields are being accepted by the American Heart Association for studies to be conducted during the year beginning July, 1953, according to Dr. Louis N. Katz, Chicago, chairman of the association's scientific council. Research fellowships are open to graduates of approved medical and graduate schools who are interested in research and who plan to follow an academic career. Established investigatorships are open to persons of proved ability who have the degree of Doctor of Medicine, Doctor of Philosophy, Doctor of Science, or the equivalent, and who are interested in a career in research. Grants-in-aid are available to nonprofit institutions for a specified program of research, including work in the basic sciences, under the direction of an experienced investigator.

The research committee recently voted to increase the stipends granted to research fellows and established investigators. Under the new scale, research fellowships, which are granted for a one year period, range from $3,500 to $5,500. Established investigatorships, which may be extended annually for a five year period, range from $6,000 to $9,000. Grants-in-aid are awarded in varying amounts, usually not exceeding $10,000, and the period covered is variable, depending on the particular program of study. Applications for research fellowships and established investigatorships should be submitted by Sept. 15. Applications for research grants-in-aid may be filed up to Dec. 1. Information may be obtained from the Medical Director, American Heart Association, 1775 Broadway, New York 19.

International Surgeons Meeting.—The annual assembly of the U. S. and Canadian chapters of the International College of Surgeons will take place at the Conrad Hilton Hotel in Chicago, Sept. 2-5. Dr. Henry W. Meyerding, Rochester, Minn., is president of the U. S. chapter and Dr. Lyon H. Appleby, Vancouver, B. C., president of the Canadian chapter. The assembly will open with a gallbladder symposium Tuesday morning. During the luncheon in the North Ballroom (11:45 a. m. to 1:45 p. m.), there will be a panel on the symposium, with Dr. Arnold S. Jackson of Madison as moderator. The Tuesday evening session will be devoted to a symposium on antibiotics. The clinic, Wednesday morning, will be followed by a roundtable discussion on treatment of duodenal ulcers, and the evening session will be devoted to a film forum. The Thursday morning program will feature recent developments in clinical research. During this session the Herbert Acuff Memorial Address on "Feasibility of Prolonged Survival Following Total Pelvic Exenteration for Advanced Cancer" will be delivered at 9 a. m. by Dr. Alexander Brunschwig, New York, and the Custis Lee Hall Memorial Address on "Volkman's Ischaemic Contraction" will be given at 10 a. m. by Dr. Meyerding. On Thursday at 4:10 p. m. there will be a roundtable discussion on surgery of the colon, rectum, and anal canal.

The speaker at the banquet, Thursday evening, is Mr. Arthur Dickson Wright, F.R.C.S., surgeon at St. Marys Hospital and

Prince of Wales Hospital, London, and a member of the council of the Royal College of Surgeons of England.

The convocation will be held at the Civic Opera House at 7 Friday evening. The Right Hon. Lord Horder, G.C.V.O., M.D., F.R.C.P., F.R.C.S., of London, England, will deliver an address on "Freedom in Medicine."

Two special features of the meeting will be the program on Tuesday of a new section devoted to the basic sciences allied to surgery, and a special program for operating room nurses.

Among the foreign surgeons who are expected to make presentations during the session are the following: Dr. Bernhard Zondek, head of the hormone research laboratory, Hadassah Medical School of the Hebrew University of Jerusalem; Dr. Raymond Darget, professor of urology at the University of Bordeaux; Dr. Lucien Leger, assistant professor of surgery, University of Paris; and Dr. Antonio Puigvert Gorro, director of the Institute of Urology, University of Barcelona.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States and its territories and possessions in the weeks ended as indicated:

Area	July 12, 1952	July 5, 1952	July 14, 1951
New England States			
Maine	3	2	1
New Hampshire	..	..	..
Vermont	1	1	..
Massachusetts	6	2	17
Rhode Island	..	..	..
Connecticut	2	2	2
Middle Atlantic States			
New York	26	24	26
New Jersey	10	2	7
Pennsylvania	8	4	11
East North Central States			
Ohio	41	45	24
Indiana	5	2	8
Illinois	33	4	40
Michigan	19	13	24
Wisconsin	5	3	15
West North Central States			
Minnesota	17	4	7
Iowa	72	27	12
Missouri	5	10	13
North Dakota	..	1	4
South Dakota	15	2	2
Nebraska	35	16	7
Kansas	19	17	8
South Atlantic States			
Delaware	..	..	..
Maryland	2	..	6
District of Columbia	5	..	..
Virginia	13	10	4
West Virginia	17	5	3
North Carolina	11	8	6
South Carolina	..	..	3
Georgia	18	11	32
Florida	38	10	18
East South Central States			
Kentucky	18	2	1
Tennessee	21	12	16
Alabama	13	17	27
Mississippi	38	26	16
West South Central States			
Arkansas	9	10	12
Louisiana	60	19	29
Oklahoma	47	26	22
Texas	296	186	92
Mountain States			
Montana	5	1	1
Idaho	3	1	..
Wyoming	1	..	2
Colorado	10	6	20
New Mexico	22	16	3
Arizona	7	7	5
Utah	..	1	2
Nevada	..	..	..
Pacific States			
Washington	18	14	5
Oregon	7	9	4
California	46	43	58
Territories and Possessions			
Alaska	..	..	..
Hawaii	11	18	..
Puerto Rico	2	..	3
Total	1,060	639	618

CORRECTION

Florida Medical Officers.—In THE JOURNAL, July 12, page 1038, Dr. Samuel M. Day, Jacksonville, was listed as editor of the *Journal of the Florida Medical Association*. Dr. Day was re-elected secretary-treasurer of the association, and Dr. Shaler A. Richardson, Jacksonville, was re-elected editor of the journal.

EXAMINATIONS AND LICENSURE

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, June 23-25. Sec., Dr. D. G. Gill, 537 Dexter Ave., Montgomery.

ALASKA:* *Examination.* Juneau. On application in other towns where there are board members. *Reciprocity.* On application. Sec., Dr. W. M. Whitehead, Box 140, Juneau.

ARKANSAS:* *Examination.* Little Rock, Nov. 6-7. Sec., Dr. Joe Verser, Harrisburg.

CALIFORNIA: *Written.* Los Angeles, Aug. 18-21; Sacramento, Oct. 20-23. Application must be received at least two weeks prior to date of examination. *Oral for Reciprocity Applicants.* Los Angeles, Aug. 16; San Francisco, Nov. 8. Applicants are requested not to arrange to come to an oral examination until they receive notice from the Credentials Committee. *Oral and Clinical for Foreign Medical School Graduates.* Los Angeles, Aug. 17; San Francisco, Nov. 9. Sec., Dr. Frederick N. Scatena, 1020 N St., Sacramento.

COLORADO:* *Reciprocity.* Denver, Oct. 14. Exec. Sec., Mrs. B. H. Hudgens, 831 Republic Bldg., Denver.

DISTRICT OF COLUMBIA:* *Reciprocity.* Washington, Sept. 8. Sec., Dr. Daniel L. Seckinger, 4130 E. Municipal Bldg., Washington.

FLORIDA:* *Examination.* Jacksonville, Nov. 23-25. Sec., Dr. Homer L. Pearson, 701 Dupont Bldg., Miami 32.

GEORGIA: *Reciprocity.* Atlanta, Oct. 14-15. Sec., Mr. R. C. Coleman, 111 State Capitol, Atlanta 3.

GUAM: The Commission on Licensure will meet whenever a candidate appears or submits his credentials. Ex. Sec., Dr. Austin W. Matthis, Agana.

ILLINOIS: *Examination.* Chicago, Sept. 23-25. Supt. of Regis., Mr. Charles F. Kervin, Capitol Bldg., Springfield.

KANSAS: Topeka, Dec. 10-11. Sec., Dr. O. W. Davidson, 864 New Brotherhood Bldg., Kansas City.

MICHIGAN:* *Examination.* Lansing, Oct. 8-10. Sec., Dr. J. Earl McIntyre, 202-4 Hollister Bldg., Lansing.

MINNESOTA:* Minneapolis, Oct. 21-23. Sec., Dr. J. F. Du Bois, 230 Lowry Medical Arts Bldg., St. Paul 2.

MISSISSIPPI: *Reciprocity.* Jackson, December. Asst. Sec., Dr. R. N. Whitfield, State Board of Health, Jackson 113.

MONTANA: Helena, Oct. 6-8. Sec., Dr. S. A. Cooney, 214 Power Block, Helena.

NEBRASKA:* *Examination.* Omaha, June 1953. Director, Mr. Husted K. Watson, Room 1009 State Capitol Bldg., Lincoln 9.

NEVADA:* Carson City, Aug. 4. Sec., Dr. George H. Ross, 112 Curry St., Carson City.

NEW HAMPSHIRE: Concord, Sept. 10. Sec., Dr. John S. Wheeler, 107 State House, Concord.

NEW JERSEY: *Examination.* Trenton, Oct. 21-24. Sec., Dr. E. S. Hallinger, 28 W. State St., Trenton.

NORTH CAROLINA: *Reciprocity.* Durham, Oct. 13. Sec., Dr. Joseph J. Combs, 419 Professional Bldg., Raleigh.

OHIO: *Reciprocity.* Columbus, Oct. 7. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus.

OREGON:* *Reciprocity.* Portland, July 25-26. Final date for filing application was June 16. Exec. Sec., Mr. Howard I. Bobbitt, 609 Failing Bldg., Portland.

SOUTH CAROLINA: *Reciprocity.* Columbia, Sept. 3. Sec., Mr. N. B. Heyward, 1329 Blanding St., Columbia.

TENNESSEE:* *Examination.* Memphis, Oct. 1-2. Sec., Dr. H. W. Qualls, 1635 Exchange Bldg., Memphis.

TEXAS: *Reciprocity.* Fort Worth, Aug. 3. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth.

WYOMING: Cheyenne, Oct. 6. Sec., Dr. Franklin D. Yoder, State Office Bldg., Cheyenne.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ALASKA: *Examination.* On application. Juneau or other towns in Territory as decided by Board. *Reciprocity.* On application. Sec., Dr. C. Earl Albrecht, Box 1931, Juneau.

ARIZONA: *Examination.* Tucson, Sept. 16. Sec., Mr. Herbert D. Rhodes, Room 423, Liberal Arts Bldg., University of Arizona, Tucson.

ARKANSAS: *Examination.* Little Rock, Oct. 1-2. Sec., Mr. Louis E. Gebauer, 1002 Donaghey Bldg., Little Rock.

COLORADO: *Examination.* Denver, Sept. 10-11. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 18.

DISTRICT OF COLUMBIA: *Examination.* Washington, Oct. 20-21. Sec., Dr. Daniel L. Seckinger, 4130 E. Municipal Bldg., Washington.

FLORIDA: *Examination.* Gainesville, Oct. 25. Sec., Mr. M. W. Emmel, Box 340, University of Florida, Gainesville.

MICHIGAN: *Examination.* Detroit and Ann Arbor, Oct. 10-11. Sec., Mrs. Anne Baker, 423 W. Michigan Ave., Lansing.

MINNESOTA: *Examination.* Minneapolis, Oct. 7-8. Sec., Mr. Raymond N. Bieter, 105 Millard Hall, University of Minnesota, Minneapolis.

NEBRASKA: *Examination.* Omaha, Oct. 7-8. Director, Bureau of Examining Boards, Mr. Husted K. Watson, 1009 State Capitol Bldg., Lincoln.

NEW MEXICO: *Examination.* Santa Fe, Sept. 21. Sec., Mrs. Marguerite Cantrell, Box 1592, Santa Fe.

OKLAHOMA: *Examination.* Oklahoma City, Sept. 13. Sec., Dr. Clinton Gallaher, 813 Braniff Bldg., Oklahoma City.

OREGON: *Examination.* Portland, Sept. 6 and Dec. 6. Sec., Dr. Charles D. Byrne, State Board of Higher Education, University of Oregon, Eugene.

RHODE ISLAND: *Examination.* Providence, Aug. 13. Administrator of Professional Regulations, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

TEXAS: *Examination.* Austin, October. Sec., Brother Raphael Wilson, 407 Perry-Brooks Bldg., Austin.

WISCONSIN: *Examination.* Madison, Sept. 13, Milwaukee, Dec. 6. Sec., Mr. W. H. Barber, 621 Ransom St., Ripon.

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* Basic Science Certificate required.

MEETINGS

ALASKA TERRITORIAL MEDICAL ASSOCIATION, Anchorage, Aug. 21-23. Dr. William P. Blanton, P. O. Box 2569, Juneau, Secretary.

AMERICAN ASSOCIATION OF OBSTETRICIANS, GYNECOLOGISTS AND ABDOMINAL SURGEONS, The Homestead, Hot Springs, Va., Sept. 4-6. Dr. William F. Mengert, 2211 Oak Lawn Ave., Dallas, Texas, Secretary.

AMERICAN COLLEGE OF SURGEONS, Waldorf-Astoria, New York, Sept. 22-26. Dr. Michael L. Mason, 40 East Erie St., Chicago 11, Secretary.

AMERICAN CONGRESS OF PHYSICAL MEDICINE, Roosevelt Hotel, New York, Aug. 25-29. Dr. Frances Baker, One Tilton Ave., San Mateo, Calif., Secretary.

AMERICAN HOSPITAL ASSOCIATION, Philadelphia, Sept. 15-18. Mr. George Bugbee, 18 East Division St., Chicago 10, Executive Director.

AMERICAN MEDICAL ASSOCIATION PUBLIC RELATIONS INSTITUTE, Edgewater Beach Hotel, Chicago, Sept. 4-5. Mr. Leo E. Brown, 535 N. Dearborn St., Chicago 10, Director.

AMERICAN PHYSIOLOGICAL SOCETY, New Orleans, Sept. 4-6. Dr. E. F. Adolph, University of Rochester School of Medicine and Dentistry, Rochester, N. Y., Secretary.

AMERICAN ROENTGEN RAY SOCIETY, Shamrock Hotel, Houston, Texas, Sept. 23-26. Dr. Barton R. Young, Germantown Hospital, Philadelphia 44, Secretary.

AMERICAN SOCIETY OF MAXILLOFACIAL SURGEONS, Hotel del Coronado, San Diego, Calif., Sept. 10-13. Dr. Casper M. Epsteen, 25 East Washington St., Chicago 2, Secretary.

BIOLOGICAL PHOTOGRAPHIC ASSOCIATION, Hotel New Yorker, New York, Sept. 10-12. Mr. Lloyd E. Varden, Pavelle Color, Inc., 533 W. 57th St., New York 19, Secretary.

COLORADO STATE MEDICAL SOCIETY, Stanley Hotel, Estes Park, Sept. 9-12. Mr. Harvey T. Sethman, 835 Republic Bldg., Denver 2, Executive Secretary.

MEDICAL SOCIETY OF DELAWARE, Rehoboth, Sept. 8-10. Dr. Andrew M. Gehret, 822 North American Bldg., Wilmington, Secretary.

MICHIGAN STATE MEDICAL SOCIETY, Book-Cadillac Hotel, Detroit, Sept. 24-26. Dr. L. Fernald Foster, 606 Townsend St., Lansing 15, Secretary.

MONTANA MEDICAL ASSOCIATION, Florence Hotel, Missoula, Sept. 18-21. Mr. L. R. Hegland, 104 North Broadway, Billings, Executive Secretary.

NATIONAL MEDICAL ASSOCIATION, Chicago, Aug. 11-15. Dr. John T. Givens, 1108 Church St., Norfolk 10, Va., General Secretary.

NEUROSURGICAL SOCIETY OF AMERICA, The Cloister, Sea Island, Ga., Sept. 18-20. Dr. C. D. Hawkes, 22 North Manassas St., Memphis 5, Tenn., Secretary.

NEVADA STATE MEDICAL ASSOCIATION, Reno, Aug. 21-23. Dr. William A. O'Brien III, 505 Chestnut St., Reno, Secretary.

NEW HAMPSHIRE MEDICAL SOCIETY, Mt. Washington Hotel, Bretton Woods, Sept. 7-9. Dr. Deering G. Smith, 44 Chester St., Nashua, Secretary.

NORTH PACIFIC PEDIATRIC SOCIETY, Challenger Inn, Sun Valley, Idaho, Sept. 19-20. Dr. S. Gorham Babson, 1107 S.W. 13th Ave., Portland 5, Ore., Secretary.

NORTH PACIFIC SOCIETY OF INTERNAL MEDICINE, Sun Valley, Idaho, Sept. 19-20. Dr. Robert L. King, 1115 Terry Ave., Seattle 1, Wash., Secretary.

NORTH TEXAS-SOUTHERN OKLAHOMA FALL CLINICAL CONFERENCE, Wichita Falls, Texas, Sept. 17. Dr. E. Aubrey Cox, Hamilton Bldg., Wichita Falls, Texas, Chairman.

RENO SURGICAL SOCIETY CONFERENCE, Reno, Nevada, Aug. 21-23. Dr. Olin C. Moulton, 130 N. Virginia St., Reno, Nevada, Chairman.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY, Denver, Aug. 7-9. Dr. Maurice D. Frazer, 1037 Stuart Bldg., Lincoln, Neb., Secretary.

U. S. CHAPTER, INTERNATIONAL COLLEGE OF SURGEONS, Conrad Hilton Hotel, Chicago, Sept. 2-5. Dr. Arnold S. Jackson, 1516 Lake Shore Drive, Chicago, Executive Secretary.

UTAH STATE MEDICAL ASSOCIATION, Salt Lake City, Sept. 4-6. Dr. T. C. Weggeland, 42 S. Fifth East St., Salt Lake City, Secretary.

VERMONT STATE MEDICAL SOCIETY, Mt. Washington Hotel, Bretton Woods, N. H., Sept. 7-9. Dr. James P. Hammond, 128 Merchants Row, Rutland, Secretary.

WASHINGTON STATE MEDICAL ASSOCIATION, Olympic Hotel, Seattle, Sept. 13-17. Dr. Bruce Zimmerman, 338 White-Henry-Stuart Bldg., Seattle, Secretary.

INTERNATIONAL

AERO MEDICAL ASSOCIATION INTERIM MEETING, Paris, France, Sept. 26-28. Dr. Armand Robert, 2 Rue Marbeuf, Paris 8e, France, Secretary.

AMERICAN CONGRESS OF INDUSTRIAL MEDICINE, Rio de Janeiro, Brazil, Sept. 20-28. Prof. Dr. Jose Pedro Reggi, Calle Arenales No. 981 Buenos Aires, Argentina, Director General.

AUSTRALASIAN MEDICAL CONGRESS, Melbourne Victoria, Australia, Aug. 22-30. Dr. C. H. Dickson, Medical Society Hall, 426 Albert St., East Melbourne, Victoria, Australia, General Secretary.

EUROPEAN CONGRESS OF CARDIOLOGY, University of London, Bloomsbury, W.C.1, England, Sept. 10-12. Dr. K. Shirley Smith, 35 Wimpole St., London, W.1, England, Secretary.

EUROPEAN SOCIETY OF CARDIOVASCULAR SURGERY, Strasbourg, France, Oct. 3-4. Sir James Learmonth, Department of Surgery, University New Buildings, Edinburgh 8, Scotland.

INTERAMERICAN CARDIOLOGICAL CONGRESS, Buenos Aires, Argentina, Aug. 31-Sept. 7. Dr. Blas Moia, Larrea 1132, Buenos Aires, Argentina, Secretary-General.

INTER-AMERICAN CONGRESS OF PUBLIC HEALTH, Havana, Cuba. Sept. 26-Oct. 1. Pan-American Sanitary Bureau, 2001 Connecticut Ave., Washington, D. C.

INTER-AMERICAN CONGRESS OF RADIOLOGY, Mexico City, Mexico, Nov. 2-8. Dr. Guido Torres Martinez, Marsella No. 11, Mexico, D.F., Secretary-General.

INTERNATIONAL CONGRESS OF ANTHROPOLOGY AND ETHNOLOGY, Vienna, Austria, Sept. 1-8. For information write: Secretaries, Royal Anthropological Institute, 52 Upper Bedford Place, London, W.C.1, England.

INTERNATIONAL CONGRESS ON DISEASES OF THE CHEST, Rio de Janeiro, Brazil, Aug. 24-30. Mr. Murray Kornfeld, 112 East Chestnut St., Chicago 11, Illinois, Executive Secretary.

INTERNATIONAL CONGRESS OF HAEMATOLOGY, Mar del Plata, Argentina, Sept. 21-26. Dr. Carlos Reussi, Anchorena 1710, Buenos Aires, Argentina, Secretary.

INTERNATIONAL CONGRESS OF THE HISTORY OF MEDICINE, Nice-Cannes, France, and Monaco, Sept. 8-14. Dr. F. A. Sondervorst, 124 Avenue des Allies, Louvain, Belgium, Secretary-General.

INTERNATIONAL CONGRESS ON HYDATID DISEASE, Santiago, Chile, Nov. 21-24. Organizing Committee, P. O. Box 9183, Santiago, Chile.

INTERNATIONAL CONGRESS OF INTERNAL MEDICINE, Friends House, London, N.W.1, Eng. Sept. 15-18. Sir Harold Boldero, 12 Pall Mall East, London, S.W.1, England, Secretary.

INTERNATIONAL CONGRESS OF MEDICAL PRESS, Venice, Italy, Oct. 4-5. Dr Bruno de Biasio, S. Marco 4646, Venice, Italy, Secretary.

INTERNATIONAL CONGRESS ON MEDICAL RECORDS, London, England, Sept. 7-12. Miss Gwen Perkins, 120 C Street S.E., Washington, D. C., Chairman.

INTERNATIONAL CONGRESS OF MILITARY MEDICINE AND PHARMACY, Montevideo, Uruguay, March 1-7, 1953. Dirreccion General del Servico de Sanitad Militar, 8 de Octubre y Mariano Moreno, Montevideo, Uruguay, Secretariat of the Congress.

INTERNATIONAL CONGRESS ON NEUROPATHOLOGY, Rome, Italy, Sept. 8-13. Dr. Armando Ferraro, 722 W. 168th St., New York, N. Y., U. S. A., Secretary General.

INTERNATIONAL CONGRESS OF OTORHINOLARYNGOLOGY, Amsterdam, Netherlands, June 8-15, 1953. Dr. W. H. Struben, J. J. Viottastraat 1, Amsterdam, Netherlands, Secretary.

INTERNATIONAL CONGRESS OF THERAPEUTICS, Madrid, Spain, Oct. 16-18. Professor Armijo, Instituto de Farmacologia, Cuidad Universitaria, Madrid, Spain, Secretary.

INTERNATIONAL CONGRESS OF UROLOGY, The Waldorf-Astoria, New York, N. Y., U. S. A., Sept. 15-18. Dr. John A. Taylor, 2 East 54th St., New York, N. Y., U. S. A., Secretary-General.

INTERNATIONAL HOSPITAL CONGRESS, London, England, May 25-30, 1953. Capt. J. E. Stone, 10 Old Jewry, London, EC2, England, Hon. Secretary.

INTERNATIONAL STUDY CONFERENCE ON CHILD WELFARE, Bombay, India, Dec. 5-12. For information write: All India Save the Children Committee, 5 Carmichael Road, Bombay, India.

INTERNATIONAL UNION AGAINST TUBERCULOSIS, Rio de Janeiro, Brazil, Aug. 24-27. Prof. Etienne Bernard, 66 Blvd. St. Michel, Paris 6e, France, Secretary-General.

MEDICAL WOMEN'S INTERNATIONAL ASSOCIATION, Vichy, France, Sept. 12-16. Dr. Margaret M. Wurts, 27 East Wellesley Road, Montclair, N. J., U. S. A., National Secretary.

NEURORADIOLOGIC SYMPOSIUM, Stockholm, Sweden, Sept. 17-20. Docent Ake Lindbom, Symposium Neuroradiologicum, Serafimerlasarettet, Stockholm K., Sweden, Secretary.

WORLD CONGRESS OF JEWISH PHYSICIANS, Jerusalem, Israel, Aug. 10-14. Secretariat: % Israel Medical Association, Rehov Mesilat Yesharim, Beth Kovatz, Jerusalem, Israel.

WORLD CONGRESS OF MEDICINE, Montecatini, Italy, Oct. 16-18. Secretariat: Corso Trieste, 65, Rome, Italy.

WORLD FEDERATION OF MENTAL HEALTH, Brussels, Belgium, Aug. 25-Sept. 1. Dr. J. R. Rees, 19 Manchester St., London, W.1, England, Secretary.

WORLD MEDICAL ASSOCIATION, Athens, Greece, Oct. 12-16. Dr. Louis H. Bauer, 2 East 103d St., New York 29, N. Y., Secretary General.

DEATHS

Beck, Carl ✠ Sayre, Pa.; born in Milin, Austria, March 26, 1864; Deutsche Universität Medizinische Fakultät, Prague, Austria, 1889; at one time assistant in surgery and gynecology in the clinics at Prague; made several trips to America as steamer surgeon in 1889-1890, settling in Chicago in the latter year to follow the general practice of medicine; served as volunteer in the 11th Infantry Regiment, Austrian Army, and later first lieutenant of the 75th Infantry Regiment; member of the military council and teacher of plastic surgery to military surgeons during World War I; for many years professor of surgical pathology and clinical pathology at the University of Illinois College of Medicine; formerly professor of surgery at the Post Graduate Hospital and Medical School and the Chicago College of Dentistry; fellow and a founder of the American College of Surgeons; past president of the Chicago Surgical Society; a founder of the German Medical Society and the Bohemian Medical Society of Chicago; member of the Illinois State Medical Society, German Society of Surgeons of Berlin, Society of Physicians of Prague, and the Royal Academy of Rome; founder and chief of staff of surgery, North Chicago Hospital; founded St. Anthony Hospital, with Sisters of Joliet; and was attending surgeon at Cook County and St. Joseph hospitals; originator of bismuth paste treatment for chronic sinusitis under name of Beck's paste; author of "Principles of Surgery," 1905, and "Crippled Hand and Arm," 1925, as well as of many articles in medical journals; died July 21, aged 88.

Brodhead, George Livingston ✠ New York; born in New Orleans Oct. 14, 1869; College of Physicians and Surgeons, medical department of Columbia College, New York, 1891; an Associate Fellow of the American Medical Association; past president of the Medical Association of the Greater City of New York; member of the New York Academy of Medicine and New York Obstetrical Society; specialist certified by the American Board of Obstetrics and Gynecology; instructor in obstetrics at his alma mater from 1895 to 1897 and the New York University and Bellevue Hospital Medical College from 1899 to 1917; professor of obstetrics at the New York Post Graduate Medical School and Hospital from 1899 to 1916; served on the staff of St. Luke's Hospital in Newburgh, Letchworth Village in Thiells, United Hospital in Port Chester, Jamaica (N. Y.) Hospital, St. Agnes Hospital in White Plains, and Knickerbocker, Jewish Maternity, Lutheran, Union, and Bronx Maternity hospitals all in New York; author of "Approaching Motherhood"; died May 13, aged 82, of bronchopneumonia.

Kemper, John Willard ✠ Ann Arbor, Mich.; born in Richmond, Ind., Sept. 14, 1891; University of Michigan School of Dentistry in Ann Arbor in 1917 and University of Michigan Medical School in 1927; joined the university staff as instructor in oral surgery in 1929; the following year became assistant professor, and in 1934 was elevated to the rank of associate professor; promoted to full professorship in 1935, and in the same year became head of the department of oral surgery and consulting dental surgeon to the University Hospital; for many years affiliated with St. Joseph's Mercy Hospital; specialist certified by the American Board of Plastic Surgery; fellow of the American College of Surgeons; first vice-president and second president of the American Society of Maxillofacial Surgeons; served during World War I; associate editor of the *American Journal of Orthodontics and Oral Surgery*; died in the University Hospital May 8, aged 60, of dissecting aneurysm of the aorta with cardiac tamponade.

Jones, Marvin Fisher ✠ New York; born in Spencer, N. Y., March 10, 1889; University of Buffalo School of Medicine, 1913; specialist certified by the American Board of Otolaryngology; at one time on the faculty of New York Post Graduate Medical School of the New York University-Bellevue Medical Center; served in France during World War I; member of the American Academy of Ophthalmology and Otolaryngology, American Laryngological Association, American Ophthalmological Society, and the American Otological Society; fellow of the American College of Surgeons; consultant, Fitkin Memorial Hospital in Neptune, N. J., Tioga County General Hospital in Waverly, New York Hospital of New York, and United Hospital in Port Chester; since 1936 surgeon-director, department of otolaryngology at Manhattan Eye, Ear and Throat Hospital, where he was in charge of its conservation of hearing service, and where he died May 26, aged 63, of multiple myeloma and cardiac failure.

Gillick, David Walter ✠ Talihina, Okla.; born in St. Louis, Aug. 9, 1895; St. Louis College of Physicians and Surgeons, 1919; fellow of the American College of Physicians; since Sept. 21, 1921, physician in the Indian Service, Department of Interior; medical officer in charge of Talihina Indian Medical Center, and during 1951-1952 was designated acting area medical officer for Eastern Oklahoma; served as superintendent and physician in charge of Shawnee Indian Sanatorium in Shawnee, and as district medical director of states, including Oklahoma, Kansas, Mississippi, North Carolina, and Florida; died in Muskogee March 29, aged 56, of cerebral hemorrhage.

Reeves, Thaddeus Benjamin ✠ Greenville, S. C.; University of Virginia Department of Medicine, Charlottesville, 1914; member of the founders group of the American Board of Surgery; for two years instructor in anatomy at his alma mater; member of the Southern Surgical Association and the Alumni Association of the Mayo Foundation; fellow of the American College of Surgeons; formerly fellow in surgery at Mayo Foundation, Rochester, Minn.; attending surgeon at the Greenville General Hospital and the St. Francis Hospital; consulting surgeon at the Shriners Hospital for Crippled Children; orthopedic surgeon for the Southern Railway and the Piedmont and Northern Railway; died June 9, aged 66.

Carlisle, Chester Lee, Palo Alto, Calif.; Western Reserve University Medical Department, Cleveland, 1898; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association and the Association for Research in Nervous and Mental Diseases; retired in July, 1946, after 15 years as clinical director of the Veterans Administration Hospital; served in state and federal hospitals for a period of 45 years; a captain in the medical corps of the U. S. Army during World War I; chief of division of mental defect and delinquency, New York State Board of Charities, from 1917 to 1920; formerly connected with the U. S. Public Health Service; died April 29, aged 75.

Kennedy, William Aloysius ✠ St. Paul; born in Minneapolis Aug. 1, 1893; University of Minnesota Medical School, Minneapolis, 1918; member of the American Academy of Ophthalmology and Otolaryngology; specialist certified by the American Board of Ophthalmology; formerly secretary-treasurer of the Minnesota Academy of Ophthalmology and Otolaryngology; served during World War I; at one time a fellow in ophthalmology at Mayo Foundation; affiliated with Children's Hospital, Gillette State Hospital, and St. Joseph's Hospital, where he died April 30, aged 58, of right amyotrophic lateral sclerosis, cerebral hemorrhage, and terminal pneumonia.

Urie, James William ✠ Wilmington, Del.; Hahnemann Medical College and Hospital of Philadelphia, 1929; served on Leyte and Luzon in the Philippines during World War II; during the campaign on Luzon was awarded the Bronze Star for heroic action in rescuing several wounded men; physician to Conrad High School football teams, and in 1950 health officer for the Memorial Hospital, where he served as secretary to hospital medical staff, and registrar for its school of nursing; affiliated with Wilmington General Hospital; died April 17, aged 46, of acute coronary thrombosis.

✠ Indicates Member of the American Medical Association.

Beer, James Anderson ✠ Columbus, Ohio; Ohio Medical University, Columbus, 1906; formerly assistant professor, university health service, Ohio State University College of Medicine; for many years city bacteriologist and at one time city health commissioner; served as treasurer of the Ohio State Medical Association; member of the American Association for the Advancement of Science; honorary member of the Columbus Academy of Medicine; died in White Cross Hospital April 30, aged 72, of cerebral hemorrhage.

Betts, George Seymour ✠ Banner, Ill.; Medical Department of Omaha University, 1898; died April 27, aged 82, of heart disease.

Breese, Floyd Pinckney ✠ Elmira, N. Y.; University of Buffalo School of Medicine, 1915; fellow of the American College of Surgeons; served during World War I; member of the honorary staff of the Arnot-Ogden Hospital; died in Coral Gables, Fla., March 16, aged 58, of acute myocardial infarction.

Brewer, Asbury Manton, Tunnel Hill, Ga.; Chattanooga (Tenn.) Medical College, 1901; died April 24, aged 79, of myocardial failure and hypertension.

Bunch, Morrell McKinsey, Muncie, Ind.; Bennett Medical College, Chicago, 1911; died April 25, aged 63.

Byram, James Waldamor, Willmar, Minn.; University of Minnesota Medical School, Minneapolis, 1931; affiliated with Willmar State Hospital; formerly affiliated with Hastings (Minn.) State Hospital; at one time a surgeon in the police department of St. Paul; died in Northwestern Hospital, Minneapolis, April 28, aged 49.

Charpentier, Albert Arthur, St. Paul; School of Medicine and Surgery of Montreal, Canada, 1899; died in Ancker Hospital April 12, aged 78, of coronary occlusion.

Creighton, Samuel Smith ✠ Colonel, U. S. Army, retired, Cambridge, Md.; University of Buffalo School of Medicine, 1909; Army Medical School, 1911; entered the medical corps of the U. S. Army in 1911, and retired Dec. 31, 1939; fellow of the American College of Surgeons; died April 3, aged 71.

Daniels, Henry Manford, Venango, Pa.; Jefferson Medical College of Philadelphia, 1887; died recently, aged 92, of uremia and arteriosclerosis.

Dimm, Charles Hill ✠ Mifflinburg, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1889; during World War I chairman of the Union County Draft Board and served as its medical examiner; died in George F. Geisinger Memorial Hospital, Danville, April 24, aged 88, of arteriosclerotic heart disease and prostatic hypertrophy.

Feldaker, Lipa M. B., St. Louis; University of St. Vladimira Faculty of Medicine, Kiev, Russia, 1922; died April 20, aged 68.

Fish, Julia F., Erie, Pa.; Pulte Medical College, Homeopathic, Cincinnati, 1901; died in Cambridge Springs, April 26, aged 86, of chronic arteriosclerotic heart disease.

Grant, John Henry, Tyler, Texas (licensed in Texas by years of practice); formerly practiced in Corpus Christi, and in 1918 was president of the Nueces County Medical Society; died April 19, aged 88.

Harris, John Simpson, McMinnville, Tenn.; University of Nashville Medical Department, 1894; Vanderbilt University School of Medicine, Nashville, 1894; died in the Vanderbilt University Hospital, Nashville, April 25, aged 84, of undiagnosed disease of biliary system with jaundice.

Harrison, Hugh ✠ Detroit; Michigan College of Medicine and Surgery, Detroit, 1896; served on the staffs of Harper and St. Joseph Mercy hospitals; died April 27, aged 80, of arteriosclerotic heart disease.

Hazen, Charles Morse, Bon Air, Va.; Medical College of Virginia, Richmond, 1897; emeritus professor of physiology at his alma mater; died April 22, aged 86, of cancer.

Heid, George Joseph ✠ Bushkill, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1906; died April 5, aged 67.

Hennemeyer, Rudolph J. ✠ Chicago; Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, 1923; affiliated with Woodlawn Hospital; died in the Albert Merritt Billings Hospital May 23, aged 56, of malignant hypertension.

Hottenstein, Daniel Edgar ✠ Millersburg, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1903; past president of the Dauphin County Medical Society; for many years county medical director; died in Harrisburg (Pa.) Hospital April 30, aged 76, of pulmonary embolism and bronchopneumonia.

Huckaby, A. H., Griffin, Ga.; University of Georgia School of Medicine, Augusta, 1905; died March 18, aged 69, of mesenteric thrombosis.

Hudnutt, Orrin Dean ✠ Plainwell, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1910; member of the Radiological Society of North America; past president of the Allegan County Medical Society; served during World War I; died in William Crispe Hospital April 25, aged 71.

Hurley, William Cyril Rowe ✠ Sunapee, N. H.; Tufts College Medical School, Boston, 1916; member of the Massachusetts Medical Society; fellow of the American College of Surgeons; for many years practiced in Quincy, Mass., where he was affiliated with Quincy Hospital; died in Sarasota, Fla., April 26, aged 63, of dissecting aortic aneurysm and coronary artery disease.

Hyde, Allan Pearson ✠ Sharon, Pa.; Cleveland Homeopathic Medical College, 1901; specialist certified by the American Board of Radiology; member of the Radiological Society of North America and the American College of Radiology; served during World War I; affiliated with Sharon General Hospital; a director of the First National Bank in Sharpsville; died April 30, aged 73, of coronary thrombosis.

Jones, Henry ✠ Coolidge, Ga. (licensed in Georgia in 1895); director of Moultrie Banking Company; affiliated with Vereen Memorial Hospital in Moultrie, where he died April 30, aged 82, of heart disease.

McNamee, John Ellis, Madison, S. D.; Barnes Medical College, St. Louis, 1902; died April 1, aged 85, of hypertensive heart disease.

Matzke, Samuel E., Warsaw, Ill.; Kansas City (Mo.) Homeopathic Medical College, 1897; affiliated with St. Joseph's and Graham hospitals in Keokuk, Iowa, and Memorial Hospital in Carthage, where he died April 2, aged 79, of carcinoma.

Moore, William Lee ✠ Madisonville, Ky.; Barnes Medical College, St. Louis, 1896; physician for the Louisville and Nashville Railroad and Illinois Central Railroad; member of the city council, 1950-1951; for many years member of the county board of health; on the staff of the Hopkins County Hospital; died recently, aged 85.

Mueller, Walter Edmund, Green Bay, Wis.; University of Illinois College of Medicine, Chicago, 1914; past president of the Brown-Kewaunee-Door Counties Medical Society; served during World War I; president of the medical staff of Bellin Memorial Hospital for many years; affiliated with Veterans Administration; died April 23, aged 61, of cirrhosis of the liver and coronary occlusion.

Murawsky, William Joseph ✠ Burlington, Wis.; Marquette University School of Medicine, Milwaukee, 1929; member of the American Academy of General Practice; health officer of Lyons; affiliated with Burlington Memorial Hospital, where he died April 23, aged 47, of cerebral hemorrhage.

Murphey, Eugene Edmund ✠ Augusta, Ga.; University of Georgia School of Medicine, Augusta, 1898; past president of the Medical Association of Georgia; fellow of the American College of Physicians; professor emeritus of clinical medicine at his alma mater; served during World War I; for many years chairman of the board of health, and city health officer; an associate member of the American Ornithologists Union; died April 13, aged 76, of pneumonia.

Nichols, James Lutellus ✠ Alligator, Miss.; Vanderbilt University School of Medicine, Nashville, Tenn., 1911; twice president of the Clarksdale and Six Counties Medical Society; served in France during World War I; died in the Kennedy General Hospital, Memphis, Tenn., April 28, aged 65, of cerebral hemorrhage.

Phillips, Floyd C. ✠ Arthur, Ill.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1902; also a graduate in pharmacy; served as president of the Douglas County Medical Society; died April 13, aged 74, of cardiorenal vascular disease.

Pieroth, John Philip, Seattle; Rush Medical College, Chicago, 1925; served during World War I; on the staff of the Virginia Mason Hospital; died April 14, aged 57, of pontine hemorrhage.

Piper, Clark Culbertson ✠ Highland Park, Mich.; Rush Medical College, Chicago, 1915; died in Highland Park General Hospital April 22, aged 65.

Portoghese, Nunzio, San Diego, Calif.; Regia Università degli Studi di Palermo. Facoltá di Medicina e Chirurgia, Italy, 1906; died April 11, aged 73, of coronary occlusion.

Price, Nathaniel Gordon ✠ Newark, N. J.; Bellevue Hospital Medical College, New York, 1897; served on the staff of Beth Israel Hospital; died in Daytona Beach, Fla., April 22, aged 75, of coronary occlusion.

Quirk, Frank John, Chicago; Bennett College of Eclectic Medicine and Surgery, Chicago, 1895; served during World War I; died in Wesley Memorial Hospital April 15, aged 82, of uremia and carcinoma of the prostate.

Ragsdale, Harrison Curtis ✠ Bedford, Ind.; Indiana University School of Medicine, Indianapolis, 1920; fellow of the American College of Surgeons; served during World War II; affiliated with Veterans Administration Hospital in Dwight, Ill.; formerly on the staff of Dunn Memorial Hospital; died in Indianapolis April 26, aged 56.

Reichbaum, Theodore ✠ Easton, Pa.; Harvard Medical School, Boston, 1925; specialist certified by the American Board of Internal Medicine; from 1929 to 1940 coroner of Northampton County; served during World War I; on the staff of Easton Hospital; died April 16, aged 55, of acute coronary thrombosis.

Rymer, Thomas Edward, Ripley, W. Va.; Starling Medical College, Columbus, 1903; for many years a member and president of the county board of education; served during World War I; died April 6, aged 76, of heart disease.

Simmons, Colon L., Hazlehurst, Miss.; Memphis (Tenn.) Hospital Medical College, 1900; past president of the Tri-County Medical Society; served as medical adviser for Selective Service during World War II; for a number of terms member of the board of aldermen of the city of Hazlehurst; on the staff of Hardy Wilson Memorial Hospital; died April 10, aged 75, of Hodgkin's disease.

Simpson, James Asa, Dallas, Texas; Vanderbilt University School of Medicine, Nashville, Tenn., 1900; fellow of the International College of Surgeons; member of the Industrial Medical Association; actively identified in National Guard units for many years; served in the Philippine Insurrection, the Spanish-American War, the Mexican Border campaign, and in France during World War I; affiliated with the War Relocation Authority in Topaz, Utah, during World War II; died April 20, aged 78, of coronary disease.

Sinkler, Samuel, Chicago; Chicago College of Medicine and Surgery, 1908; also a dentist; died in the Albert Merritt Billings Hospital April 25, aged 74, of hydronephrosis and bronchopneumonia.

Smith, French Miles ✠ Lyndon, Kan.; University Medical College of Kansas City, Mo., 1909; secretary of the Osage County Medical Society; died in Kansas City, Kan., April 19, aged 73, of carcinoma of the pancreas.

Starks, John Charles ✠ Gower, Mo.; Missouri Medical College, St. Louis, 1897; an Associate Fellow of the American Medical Association; died March 21, aged 77, of coronary occlusion and arteriosclerosis.

Stein, Frederick ✠ Lyndhurst, N. J.; L.R.C.P., Edinburgh, L.R.C.S., Edinburgh, and L.R.F.P. & S., Glasgow, 1941; associate dermatologist, St. Mary's Hospital in Passaic; died April 21, aged 40, of coronary occlusion.

Stine, Harvey Andrew ✠ Harrisburg, Pa.; Baltimore Medical College, 1912; consultant in obstetrics, Harrisburg Polyclinic Hospital; died April 4, aged 73, of myocardial infarction and arteriosclerosis.

Van Doren, Raymond Fleming ✠ East Lynn, Ill.; Northwestern University Medical School, Chicago, 1911; an Associate Fellow of the American Medical Association; died May 5, aged 65, of cardiorenal disease.

Van Gundy, Clyde Rogers ✠ Detroit; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1912; served overseas during World War I; on the staff of the Lincoln Hospital; died May 5, aged 65, of coronary thrombosis.

Vella, Salvatore I., Chicago; Chicago College of Medicine and Surgery, 1915; died in St. Luke's Hospital April 22, aged 64, of cerebral thrombosis, hypertension, and diabetes mellitus.

Vincil, Frank Hendricks, Portland, Ore.; Barnes Medical College, St. Louis, 1903; served during World War I; died in Veterans Administration Hospital April 30, aged 72, of coronary sclerosis and diabetes mellitus.

Vinson, Charles Samuel ✠ Columbus, Ohio; Ohio State University College of Medicine, Columbus, 1941; served overseas during World War II; resident in radiology at Ohio State University Hospital, where he died April 28, aged 35, of coronary infarction.

Vogt, Elkin ✠ Lithonia, Ga.; University of Georgia School of Medicine, Augusta, 1939; member of the American Academy of General Practice; died May 5, aged 49, of coronary thrombosis.

Wagner, Louise Dorothy ✠ Santa Barbara, Calif.; Rush Medical College, Chicago, 1920; for many years practiced in Pasadena, where she was affiliated with Huntington Memorial Hospital; died in Santa Barbara Cottage Hospital April 2, aged 56, of carcinoma of the sigmoid.

Wagner, Nicholas Bacon, Platteville, Wis.; Rush Medical College, Chicago, 1910; died May 19, aged 73.

Wentz, Frank Riegel ✠ Allentown, Pa.; Jefferson Medical College of Philadelphia, 1913; affiliated with Sacred Heart Hospital, where he died April 25, aged 60, of myocardial infarction.

Whelan, Joseph David ✠ Manchester, N. H.; Georgetown University School of Medicine, Washington, D. C., 1934; served during World War II; chief of staff, Sacred Heart Hospital; died in the Veterans Administration Hospital, Boston, May 6, aged 44, of leukemia.

Whitaker, Leslie Stow ✠ San Jose, Calif.; University of Louisville (Ky.) School of Medicine, 1926; affiliated with Santa Clara County Hospital and O'Connor Hospital; died May 10, aged 52, of coronary occlusion.

Williams, Dell E., Laguna Beach, Calif.; State University of Iowa College of Medicine, Iowa City, 1897; died April 29, aged 80, of cardiac decompensation.

Willis, David Arthur ✠ Chicago; University of Illinois College of Medicine, Chicago, 1923; associate professor of surgery, Chicago Medical School; specialist certified by the American Board of Surgery; fellow of the American College of Surgeons; affiliated with Mount Sinai Hospital; died in the Garfield Park Community Hospital May 19, aged 52, of myocardial infarction.

Ziegler, Samuel Edgar, Piqua, Ohio; Starling-Ohio Medical College, Columbus, 1910; died March 8, aged 78.

GOVERNMENT SERVICES

ARMY

Promotions in the Surgeon General's Office.—Stars were pinned on two officers of the Medical Service in a ceremony July 7 in the Surgeon General's Office. Major Gen. Silas B. Hays, Deputy Surgeon General, was awarded his second star and Col. Rawley E. Chambers, newly appointed Chief of Professional Divisions in the Surgeon General's Office, became a brigadier general.

General Hays became Deputy Surgeon General last year after serving as surgeon of the Japan Logistical Command since early in the Korean conflict. In this assignment he was responsible for management of Army hospitals in Japan, evacuation of casualties from Korea, and furnishing of medical supplies and equipment to both Japan and Korea. During World War II General Hays served as chief of medical supply in the European Theater of Operations. He was awarded the Legion of Merit with Oak Leaf Cluster, the Croix de Guerre with Palm, and Order of Public Health from France for his work in that country.

In addition to being coordinator of seven professional divisions in the Surgeon General's Office, General Chambers will serve as chief of the psychiatry and neurology consultants division. He has served as chief of the neuropsychiatric service at Brooke Army Hospital, Fort Sam Houston, Texas, and director of the department of neuropsychiatry at the medical field service school there. Under his direction the child guidance clinic was created at the hospital. During World War II he was commanding officer of the 12th Evacuation Hospital, 805th Hospital Center, 77th Station Hospital, 7th General Hospital, and 7th Hospital Group in the European Theater. Among his awards are the Legion of Merit, World War II Victory Medal, and Commendation Ribbon.

NAVY

Physicians Needed for Marine Reserve Unit.—The First Engineer Battalion, Marine Corps Reserve, at Fort McHenry, Baltimore 30, offers an exceptional opportunity to physicians of the Navy Reserve. This unit is authorized to have two reserve physicians. Membership in the unit will afford physicians an opportunity to earn retirement and promotion credit points and will not effect their status in regards to active duty. However, for physicians who do not desire to attend the two week summer training camp at Camp Lejeune, N. C., but who desire to affiliate with this unit, the status of appropriate duty is offered. In an appropriate duty status a physician receives the same benefits, but is not considered a member of the unit and will not attend summer camp. Navy Reserve physicians interested should telephone Lieut. Col. E. P. Moses Jr., Marine Corps, at PLaza 4132 or see him personally at Fort McHenry in Building 1.

Reserve Officers Receive Retirement Credit for Attending Convention.—The chief of naval personnel announces that Reserve Medical Department Officers will receive retirement point credits for attending the annual convention of the Association of Military Surgeons, meeting in Washington, D. C., Nov. 17-19, 1952. Reserve officers of the Medical, Dental, Medical Service, Nurse, and Hospital Corps, not on the inactive status list (Public Law 810, 80th Congress), will receive one retirement credit point for each of the three sessions attended, provided that the duration of the meeting is at least two hours. An officer designated by the chief of the Bureau of Medicine and Surgery will attend the convention and record the names of those attending, the sessions attended and the duration of each session.

Personal.—Rear Adm. Lamont Pugh, Surgeon General of the Navy, has been notified of his recent election to active fellowship in the American Surgical Association.

PUBLIC HEALTH SERVICE

Regular Corps Examination for Medical Officers.—On Oct. 7, 8, and 9, 1952, the U. S. Public Health Service will hold competitive examinations for physicians interested in appointment in the Regular Corps. Completed applications, accompanied by a birth certificate and transcripts, must be received in the Washington office no later than Aug. 26. Appointments are for career service and will be made in the grades of Assistant and Senior Assistant Surgeon, with salary and allowances totaling $6,017 and $6,918, respectively. Provisions are made for periodic promotion, liberal retirement benefits, sick and annual leave, and other benefits. Applicants must be citizens of the United States and graduates of a recognized school of medicine. Interns are eligible for admission to the examination. Additional information should be requested immediately from the Chief, Division of Commissioned Officers, Public Health Service, Federal Security Agency, Washington 25, D. C.

Survey of Equipment and Supplies for Hospitals.—Half of the nation's hospitals have completed and returned their questionnaires in the nation-wide survey of the needs of civilian hospitals for vital equipment and supplies, it was announced by the Surgeon General. The survey is being conducted by the American Hospital Association and the Public Health Service to provide information on the supply and equipment needs of hospitals as a basis for determining what production is required to meet these needs. With this information, the equipment and supply requirements of the nation's medical care facilities can be planned more accurately as military requirements rise. Wesley E. Gilbertson, chief of the Public Health Service's Division of Civilian Health Requirements, urges that hospitals that have not yet returned the questionnaire do so immediately.

It was emphasized that reliability of the survey will be helped if hospital administrators will (*a*) verify that the items reported are exactly the same as those requested on the questionnaire form, (*b*) make sure that each box in the heading on the form contains an entry, (*c*) convert information respecting quantities to the units of measure requested, and (*d*) carefully review the completed questionnaire before mailing, to eliminate typographical and other inadvertent errors.

Division of Occupational Health.—New staff appointments have been announced by the Division of Occupational Health, Public Health Service, coincident with the reorganization of the division that went into effect on July 1. The environmental investigations branch and the clinical investigations branch have been merged into a single investigations branch at Cincinnati, which will be headed by Dr. W. Clark Cooper. Dr. Cooper was formerly Deputy Chief of Medical Services in the Public Health Service Hospital, San Francisco. Dr. Dale C. Cameron, who had previously served as chief of the cooperative health services branch, is now in charge of the new program developments branch of the division. Mr. Henry Doyle, who was formerly in charge of the division's Salt Lake City field station, will direct the activities of the state aid branch. Both of these branches are located in the Washington office. Dr. Lewis J. Cralley has been assigned to direct the activities of the Salt Lake City field station. Prior to this new assignment, Dr. Cralley had served as chief of the environmental investigations branch in Cincinnati.

Field Work for Foreign Health Workers.—The Division of International Health of the Public Health Service recently assisted the Rockefeller Foundation and the World Health Organization in orienting into the field of public health two groups of foreign health workers who just graduated from various schools of public health in the United States. The students, who represented 18 different countries, were given field work in Mississippi, Georgia, and Tennessee. Following this they were placed in county health departments in five states for further training during the summer.

FOREIGN LETTERS

ARGENTINA

Congress of University Teachers.—From May 14 to 17 the first Congress of University Teachers was held in Buenos Aires. In Argentina there are only governmental universities, private ones not being allowed. In one of the initial speeches, President Perón was mentioned as the "archetype of the University professor." At the final meeting, the congress declared that the mission of Argentine universities is to promote and diffuse a national culture related to the Christian occidental civilization and in accordance with the national constitution. The congress requested that the rank of full professor be considered at the same economical rank of a judge and that the function of professor be incompatible with any other official position. The congress established 169 technical committees for the study of university problems. The congress asked that May 15 be declared the "day of the University teacher" and that the Confederation of University Teachers be called for an international university congress under the economic support of the government. President Perón delivered a speech at the final meeting of the congress.

Prizes Awarded.—The prize of the Severo Vaccaro Foundation (1951-1952) was awarded to Dr. Oscar Orias, director of the Mercedes and Martin Ferreyra Institute for Medical Research, a private scientific nonprofit laboratory in Cordoba, supported by public gifts and in great part by resources granted by many Rotary Clubs of Argentina. Dr. Orias was a pupil of Professors C. Wiggers (Western Reserve), W. B. Cannon (Harvard), and B. A. Houssay (Buenos Aires), and was visiting professor of physiology in Long Island College of Medicine from 1948 to 1949. His principal researches have been on heart dynamics in coronary ligation, experimental and clinical branch blocks, gallop rhythm, and hypertension. He wrote, with E. Braun-Menendez, a book on heart sounds, which has been translated into English. He has developed modern scientific methods for all the cardiologists of Argentina. His researches on hypophysis are very important, including studies of action on heart and blood pressure and regulation of sexual function in batrachians. With his pupil Ines de Allende he recently wrote a book "Cytology of Human Vagina," translated by Dr. George Corner. Dr. Orias has been a hard worker, a brilliant and stimulating teacher, and a man of the highest integrity and energy, who has devoted full time to research and teaching.

The annual prize of the Circulo Medico de Rosario was awarded to Drs. J. J. Staffieri and L. J. Cardonnet for clinical work on NPH 50 (modified protamine) insulin. The Argentine Medical Association awarded the Guillermo Rawson prize to Dr. J. C. Loza Colomer for his paper on "Organization of General Hospitals" and the Pedro O. Bolo prize to Drs. A. Lanari, M. Molins, and O. C. Croxatto for their experimental work on pulmonary graft. The prizes for the best medical thesis in 1951 were awarded to Drs. R. R. Rodriguez, M. A. Pico, and Gil Marino by the School of Medicine of the University of Buenos Aires.

Finlay Commemoration.—The Ministry of Public Health has organized many ceremonies in commemoration of the historical discovery by Carlos Finlay from Havana, Cuba, of the mosquito as a transmitter of yellow fever. In a ceremony attended by Pres. Juan Perón, held on May 20, a bust of Finlay was unveiled in the Policlinico Central. Moreover, one street in Buenos Aires has been named Carlos Finlay.

The items in these letters are contributed by regular correspondents in the various foreign countries.

ISRAEL

Superinfection of Leishmania Tropica in Leishmaniasis.—Successful experimental superinfection of Leishmania tropica in patients with relapsing cutaneous leishmaniasis has been performed by Dostrovsky, Sagher, and Zuckermann of the dermatological department of the Hadassah University Hospital in Jerusalem. L. tropica in a susceptible human subject ordinarily produces a lesion that heals totally and spontaneously, leaving no residual parasites. The cured host generally remains immune for life and is refractory to natural reinfection. A small percentage of patients, however, are unable to eradicate the parasite, and their initial lesions continue to grow for years owing to successive relapses, with active peripheral foci surrounding a central scar. This lesion is known as leishmaniasis recidiva.

The investigators attempted to determine whether such patients with relapsing cutaneous leishmaniasis were susceptible to experimental superinfection with cultures of a strain of L. tropica capable of inducing typical primary nodular cutaneous lesions in subjects not previously exposed to leishmania organisms. Six patients with leishmaniasis recidiva, therefore, received intradermal inoculations consisting of 1 to 10 million washed culture flagellates of L. tropica over the left and right deltoid regions, respectively. Aspirated juice from the lesions developing at the inoculation sites yielded positive cultures in five of the six patients 1 to 15 weeks after inoculation, proving the subjects susceptible to superinfection.

Superinfection lesions obtained in these patients closely resembled relapse lesions and not initial (nodosa) lesions, as shown by the following lines of evidence. 1. Superinfection and relapse lesions consisted of yellowish-brown infiltrates with peripheral "apple jelly" nodules of granulation tissue revealed by diascopic pressure, as contrasted with typical nodosa lesions, which are reddish-blue and have no apple jelly nodules. 2. Superinfection lesions, like relapse lesions, were composed of tuberculoid tissue from their inception until cicatrization, as contrasted with the histocytic structure of the typical nodosa lesion. 3. As in relapse lesions, very few parasites were found at the superinfection sites. Microscopic examination was regularly negative, and not all tubes seeded with tissue juice yielded positive cultures. In contrast, parasites are generally numerous enough in the primary nodosa type lesion to be demonstrated microscopically, and all tubes seeded from such lesions are regularly positive. This phenomenon consisting in the development of a lesion resembling the relapse type rather than the primary type at the site of superinfection in patients suffering from relapsing cutaneous leishmaniasis has been designed as an "isophasic reaction."

Diagnosis of Leprosy.—The long incubation period of leprosy is the greatest obstacle in the exact diagnosis of this disease. Through the experimental studies of Sagher, Kocsard, and Liban, it has now become possible to answer the question of whether there is an acute infection. The first observation brought the result that histological examinations following tuberculin, leishmanin, milk, and peptone injected in the skin of leprosy patients showed the development of a granulomatous reaction indistinguishable from lepromatous leprosy. Furthermore, inoculations of BCG vaccine in leprous patients produced clinically typical lesions. The histological examinations from these lesions, however, revealed a granulomatous tissue reaction indistinguishable from true lepromas. It seems, therefore, that lepromatous leprosy produces only its own histopathological response notwithstanding the cause of the lesion produced. These facts may be of importance for criteria of cure from this disease, since the response was still present in patients after disappearance of

clinical signs and bacilli. Further, early cases may be detected even in the incubation period by performance of those tests and histological findings of lepromatous granulation tissue. So far, no other known disease reacts in this way.

Antimalaria Work.—According to Dr. J. Saliternik, the annihilation of Anopheles mosquitoes is found to be the most effective method of controlling malaria in this country. The most important malaria vectors today are the Anopheles sacharovi and Anopheles sergentii. Till 1945 Anopheles sacharovi, a domestic mosquito, was considered the main malaria vector. Since then it has decreased in number as well as in importance, as a result of the use of D.D.T. sprayed systematically in all malarious districts. The most dangerous mosquito in the country today is the Anopheles sergentii. Being a half domestic mosquito it cannot be sufficiently affected by residual sprayings.

A survey of all the water courses, potential Anopheles mosquito breeding places, in this country showed: 17,878 wells, 558 natural water courses of 1,236 km., 7,500 dunams of swamps (not including the Hule), and 23,467 dunams of fish ponds. In 1950, 28,000 working days were invested for chemical and technical treatment.

The fight against the adult Anopheles mosquito is carried on by residual D.D.T. spraying (5% D.D.T. solution in gasoline). In 1950, 412 tons of D.D.T. solution were used in spraying 344 settlements in malarious districts, comprising 105,714 rooms and a population of 152,690. Antimalaria work is carried on in accordance with climatic changes, population movements, the biology of the various Anopheles species, and periodicity of the malaria seasons.

As a result of the systematic antimalaria work, there has been not only a marked reduction in the number of new malaria cases (in 1950 only 842 cases were registered), but the whole epidemiological picture was completely changed. Formerly, there were two peaks in the malaria curve, one in spring in the coastal regions in particular, caused by Anopheles sacharovi, and the second in autumn in the interior of the country, where the main vectors are Anopheles sergentii and Anopheles superpictus. Now with the reduction of Anopheles sacharovi the first peak has nearly completely disappeared, and in the second there has been a considerable decrease, too.

New Department of Anatomy.—The Hebrew University-Hadassah Medical School formally inaugurated its new department of anatomy in the presence of a large number of teachers and students. The dean of the school, Professor Dostrovsky, explained that exceptional prominence was being given to the inauguration of the courses in anatomy not only because it is a basic subject in the study of medicine but also because its inclusion in the curriculum is a vital matter for the school itself. The many difficulties inherent in giving anatomy courses in Israel have been surmounted owing to the help extended by the ministries of health and justice and by the Anatomy Law. The opening lecture was given by Dr. M. Izkovitz, lecturer in anatomy, who described the history and development of that science through the ages. Just three years after the opening of the Hebrew University-Hadassah Medical Faculty in Jerusalem, the first class of 62 students received their Doctor of Medicine degrees in May, 1952.

New Tuberculosis Center Near Jerusalem.—The formal opening of the Eytanim tuberculosis center at Deir Amr in the Jerusalem Corridor took place in May, 1952. The 225 bed hospital has a children's section, which already cares for 100 patients. It is named in the memory of the late King Christian X of Denmark. Most of the funds necessary to equip the section were contributed by the Danish government and Danish citizens. The Danish minister to Israel, Mr. Hans P. Hoffmeyer, and representatives of the Danish Jewry attended the opening ceremony.

During the inspection of the hospital, Dr. Y. Chasis, head of the health ministry's tuberculosis department, disclosed that about 4,000 persons suffered from tuberculosis in Israel, although, as in every country, no exact figure is available since not all ill persons report to the authorities. Israel has at present 108 beds per 100,000 population, but it plans to raise the number of beds to 130. This figure can be considered very favorable when compared with most other countries in the world.

The Eytanim center will be expanded to hold 300 beds. Using an idea developed successfully in Switzerland, a number of prefabricated huts have been set up for former adult patients who wish to work for the hospital after their discharge as patients. By this method it is hoped that the shortage in personnel will be overcome. At present, the personnel numbers 0.5 per bed, while the international standard is 0.7.

NORWAY

Laboratory Control of BCG Vaccine.—Last May the University of Bergen conferred an M.D. degree on Dr. E. F. Krohn for his work there on the laboratory control of BCG vaccine. His work is published as "Supplement 30" to *Acta tuberculosea Scandinavica*. The cost of his investigations, which were prompted by the director of the laboratory, Dr. J. Böe, was borne by the Norwegian National Association Against Tuberculosis. The effects of the vaccines on human beings examined by Krohn were controlled by the tuberculosis department of the Oslo Public Health Service and by the state photofluorographic service. The first BCG culture was brought to Bergen by Birkhaug in 1937 from the Pasteur Institute in Paris, and both the strains employed by Dr. Krohn were derived from a culture obtained in 1945 from the same institute. The Bergen laboratory issues two types of vaccine, one concentrated and containing 20 mg. BCG moist weight per ml., and one diluted to contain only 1 mg. BCG per ml. Krohn's investigations were concentrated on the latter, which is intended for intracutaneous injection.

Since the success of the BCG campaign throughout the world must ultimately hinge on the reliability of the laboratory control of the vaccine, Krohn's work may be said to be of vital importance to millions. Yet it is so highly technical that most of his book will be understood by only a few of his fellow workers. But even for persons to whom mathematical formulas and the finesse of laboratory technique mean little, there is much in this book to stimulate and interest them. Dr. Krohn has come to the conclusion that no definite correlation can be established between the number of viable bacillary particles and the effects of the vaccine on human beings. "Such effects would seem, accordingly, to be determined in the main by qualitative properties, the demonstration of which is not possible by ordinary laboratory methods, but will require biological tests." A series of investigations of the immunizing effects of Norwegian BCG vaccine on mice is being planned as part of the present study. They are still at a preparatory stage and will therefore be published separately. In the present work a summary after each chapter and a comprehensive summary at the end of the book are helpful in giving a bird's-eye view of Dr. Krohn's main conclusions. His bibliography contains 172 references.

Fewer Days in Hospital.—There is a general impression, not always substantiated by reliable statistical evidence, that in countries with a high cultural level patients spend fewer days in the hospital than they did a few years ago. Herr E. W. Østberg, who is attached to a statistical bureau run by the municipal authorities of Oslo, has recently provided such evidence on the basis of 11,548 patients treated in certain hospitals in Oslo during the years 1928, 1937, and 1947. During this 20 year period, the average duration of treatment in a hospital was reduced from 28.9 days in 1928 to 20.6 in 1937 to 19.9 in 1947. It will thus be seen that this reduction was much greater in the first than in the second decade under review. Since it can be assumed that the duration of treatment in the hospital rises with the average age of the patients and since the average age of the patients has risen in this 20 year period, this reduction in the duration of treatment in hospitals is, indeed, a remarkable achievement. The relative upward shift of old persons in a given community was estimated in 1948 to be such that in 1920 only

3.3% of the total population of Oslo was 70 years old or older, whereas the corresponding figure in 1948 was 5.8%. In 1928, approximately one-third of the male patients studied by Østberg were under the age of 30, whereas in 1937 they represented only 20.1% of all the male patients, and in 1947 only 13.9%. A classification of the patients according to the diseases for which they were treated in the three years under review showed that there was a relative rise in the number of cases of heart disease. This rise may well reflect the greater average age of the patients. Between 1937 and 1947 there was a marked rise in the relative frequency of all forms of pneumonia.

Education in Mental Hygiene.—The Norwegian Mental Hygiene Association, whose chairman is Dr. Gordon Johnsen, last May launched a mental hygiene education campaign with two main interests. One of them is the child of preschool age and its home. The other is the employer and the employee and the parts they play in industry. Speaking on the first subject, Dr. Johnsen pointed out that the only mental hygiene polyclinic for children in Oslo has so many requests for service and so long a waiting list that up to three months have to pass before some cases can be dealt with. Yet this polyclinic is threatened by closure for want of the necessary funds. Dr. Johnsen said that the Mental Hygiene Association is planning the creation of several more polyclinics along similar lines. With the help of such powerful voluntary organizations as the National Association Against Tuberculosis and for Health, as well as the Red Cross, he hopes to organize mental hygiene teams composed of psychiatrists, psychologists, and social workers. He assured his audience that psychic disturbances were just as common in children of the preschool age as among adults.

Speaking on the same occasion, Dr. Karen Margrethe Simonsen, who was recently imported from Denmark to take charge of the new psychiatric department for children at the Rikshospital in Oslo, compared the mentalities of Norwegian and Danish children. She has come to the conclusion that in Norway the most common cause of faulty mental development in the child is the strait-laced and inhibited outlook of the parents. Inhibited by moral scruples in their emotional lives, they are apt to impose an excess of moral responsibility on their children who develop compulsion neuroses in consequence. She has found cases of this type to be much commoner in Norway than in Denmark whose population has a more open and less inhibited emotional outlook. At the Rikshospital about half of all her patients are children under school age. She is convinced that treatment given early enough, during the first years of life, has an influence on the subsequent development of the personalities of such children.

Opening of Audiological Institute in Oslo.—On May 21 the new Audiological Institute within the framework of the Rikshospital in Oslo was opened formally by the university's rector, Herr F. Castberg. It is the only institute of its kind in Norway, and it owes its creation to the generosity of a whale oil magnate, Herr Anders Jahre, whose donation of 150,000 k. has been supplemented by the sum of 75,000 k. for working expenses during the first five years. The institute is linked up with the ear, nose, and throat department of the Rikshospital, in the new surgical block. Professor Opheim, who is in charge of this department, pointed out at the opening ceremony that there are some 60,000 persons in Norway who are completely deaf, and that about 10% of the whole population suffer from defective hearing. Yet in spite of the enormous social problems raised by this form of invalidism, it was only in recent years that attempts had been made to solve them on a medical and scientific basis. The nucleus of the institute consists of a laboratory and three soundproof rooms.

The publicity given to the problems of noise and deafness in both the lay press and the medical press in recent years reflects the active interest now being taken in the prevention of defective hearing. Dr. S. Quist-Hanssen has recently published studies on this subject and has shown how much the success of ear plugs depends on the care with which they are fitted. Audiometric control of such fitting requires only a few minutes and, when supplemented by instruction in the use of such plugs, should do much to assure their success. Glass fiber wool has gained favor since an account of its use was given in May, 1951, in Helsingfors at the Scandinavian Congress for Industrial Medicine. Made from melted glass, the diameter of its fibers is only about one-tenth of that of cotton wool fibers. Dr. Quist-Hanssen has found no great difference in the effects of glass fiber wool according to whether it was lightly or tightly compressed, but other observers disagree with him on this point. A drawback to this preparation is, in his opinion, its tendency to deposit some dust in the ear passages. But they do not become irritated even when the glass fiber wool is used daily for several months. Its cheapness is also a point in its favor. It is with this problem and many others that the institute in Oslo will now be working.

TURKEY

Schistosoma Haematobium Investigation.—The Ministry of Health and Social Assistance appointed Prof. Zühdi Berke and microbiologist Dr. Tahsin Berkin of the Refik Saydam Central Institute of Hygiene, Ankara, to report on Schistosoma haematobium in the southern provinces that border Syria and Iraq. In 1939 an increase in schistosomiasis in Syria was noticed. French regiments from the Senegal, who had been stationed there from 1936 to 1941, and 60 to 70% of the Syrian population along the Syrian-Turkish border became infected. As a result of an investigation made by specialists from the Syrian Ministry of Health and in cooperation with experts from the American Medical School in Beirut, tentative control was instituted in 1948. Investigation by Prof. Zühdi Berke and Dr. Tahsin Berkin revealed the presence of two Schistosoma haematobium centers near the Turkish border. One center was in the Kuburelbeyd village, population about 1,000, 15 miles south of the Turkish border, and also in the Tel Hasnak village, 3 miles from the Turkish border. The second center was in the Tel Abyad village, 125 miles east of Halep (Aleppo) and south of the Turkish district of Akça Kale, population about 76,000, and in almost 1,000 other villages. Three streams traverse this territory. Along the Djerrahi River, from 8 to 34% of the population were affected, along the Sublah River 15 to 24%, and along the Katraniye River 10 to 40%. All patients were given treatment. Under the direction of an expert from Egypt, a schistosome prevention and control unit was equipped with a mobile hospital and laboratory to take up its activities in this territory. Investigations along the Turkish-Iraqian border confirmed that urinary schistosomiasis is endemic in Iraq. During the hot summer season, June to October, the population bathes in the streams and rivers spreading infection. Ponds and swamps, resulting from inundations, water plants along slowly moving rivers, and rice fields favor the propagation of infected snails.

Hospitals, dispensaries, and health propaganda in Iraq have resulted in a reduction of schistosomiasis and prevented more serious outbreaks. The economic aspects of the damage caused by snails has been investigated by Mr. John Watson, an expert who recommended more radical measures, and the World Health Organization has decided on an effective program for the control of the schistosomiasis scourge.

According to the report the Ministry of Health received from Prof. Berke and Dr. Berkin, there are no persons affected with schistosomiasis in the Turkish border districts of Akça Kale, Idil, and Nusaybin, or in the surrounding areas. Random urinalyses on hundreds of adults and children had negative results. Investigation at the Central Institute of Hygiene, Ankara, of mollusks from the streams and rivers traversing the three territories revealed that they were not Schistosoma haematobium hosts, Bulinus contortus, nor, though they were found in the Suruc Stream, were they infected. This corroborated the findings of Dr. Fehmi Derbent, who, in cooperation with local municipal health officers, had previously made an investigation for the Ministry of Health.

CORRESPONDENCE

TOUR TO WORLD MEDICAL ASSOCIATION MEETING IN ATHENS

To the Editor:—To facilitate travel to the Sixth General Assembly of The World Medical Association, in October, 1952, World Travel Plan has arranged a guided tour by airplane charted through an internationally known scheduled airline, namely, Sabena Airlines.

The trip will include tours of Rome, Geneva, and Paris, as well as a stay in Athens during the period of the General Assembly. The total cost is $789.00 per person, which is about $250.00 per person less than the cost of a round trip by air alone. The $789.00, however, does not include expenses in Athens, which will be in addition to the above amount. The proposition would seem to be advantageous to those who are contemplating the trip and who would like to make the tours of the other cities at the same time.

The itinerary for this tour is as follows.

DATE	PLACE	ITINERARY
Wed., Oct. 8	At New York	Accommodation provided at Hotel Roosevelt, Madison Ave. at 45th St., New York City.
Thu., Oct. 9	Leave New York	After breakfast at hotel, final check of documents and discussion. Transfer by private motor direct to Idlewild International Airport. Check in at airport and leave early afternoon by first-class D.C.-6 plane of Sabena Belgian Airlines. All meals with beverages included.
		GREECE
Fri., Oct. 10	Arrive Athens	Arrive afternoon. Transfer by private motor to hotel.
Sat., Oct. 11 to Fri., Oct. 17	At Athens	Attending the Sixth General Assembly of the World Medical Association.
Sat., Oct. 18	Leave Athens	After breakfast, transfer by motor direct to airport. Leave Athens by plane.
		ITALY
	Arrive Rome	Arrive about noon. Transfer by motor to hotel. Afternoon: A general drive and survey of the city, returning to the hotel for dinner.
Sun., Oct. 19	At Rome	This morning is available in Rome for individual action. Afternoon: Special drive to Tivoli, proceeding along the Via Tiburtina to Acqua Albule (sulfur baths), Ponte Lucano, Tomb of Plautius Lucanus to Hadrian's Villa. Continue to the Villa d'Este (visit the grounds with many fountains, artificial grottos, and pavilions); drive to the Temples of Vesta, Sybil, and Hercules and to the waterfalls of the Anio. Return to Rome for dinner.
Mon., Oct. 20	At Rome	This morning is free in Rome. Afternoon: A general drive and survey of the city.
Tue., Oct. 21	At Rome	This day available for individual action.
Wed., Oct. 22	Leave Rome	After breakfast, transfer by motor direct to airport. Leave Rome by plane.
		SWITZERLAND
	Arrive Geneva	Arrive early afternoon. Transfer by motor to hotel. Balance of day free.
Thu., Oct. 23	At Geneva	Survey of the city, then by lake steamer on Lake Geneva (Swiss and French side) including Montreux (Chillon Castle) and Lausanne.
Fri., Oct. 24	Leave Geneva	After breakfast, transfer by motor direct to airport. Leave Geneva by plane.
		FRANCE
	Arrive Paris	Arrive about noon. Transfer by motor to hotel. Afternoon by motor for a special tour of this fabulous city.
Sat., Oct. 25	At Paris	After breakfast, by motor for additional city touring. Continue to Versailles for luncheon and visit the famous palace. Back to the hotel for dinner.
Sun., Oct. 26	At Paris	This day available for individual action.
Mon., Oct. 27	At Paris	Full day free for shopping (expert guide provided). Fashion show, additional local visits, or special interest program. Special luncheon provided at famous Parisian restaurant.
Tue., Oct. 28 and Wed., Oct. 29	At Paris	Days free. Tickets provided for Folies Bergère or similar show, the opera, etc.
Thu., Oct. 30	Leave Paris	Transfer by motor direct to airport for overnight flight home. All meals provided.
		UNITED STATES
Fri., Oct. 31	Arrive New York	Arrive International Airport. Motor transportation provided into New York City.

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"TELEVISION NECK"

To the Editor:—For many years, I have had a special interest in musculoskeletal disorders. As part of every physical examination, I have measured joint mobilities according to the methods described in my monograph "The Common Form of Joint Dysfunction" (Brattleboro, Vt., E. L. Hildreth & Co., 1949).

Recently I have observed a clinical syndrome in persons who, in watching television programs, maintain strained postures of the head and neck, often for prolonged periods. The manifestations of this syndrome, which for want of a better name can be called "television neck," include measurable increased limitation in ranges of neck movement and pain or discomfort in the posterior nuchal region (with or without radiation of pain or discomfort into the shoulders, upper back, or occiput). In many of these patients, the faulty sitting and erect posture that is maintained when they are not viewing television is a result of the tendency to flex the neck on the trunk and extend the head on the neck to maintain the face roughly parallel to the frontal plane of the body and to the television screen. There is also some concomitant exaggeration of the upper dorsal curvature, suggesting a mild or moderate upper dorsal kyphosis. When television neck occurs in both husband and wife and each has a favorite chair and position for viewing television, the limitation in movement and the discomfort occur mainly on one side in the husband and on the other side in the wife.

When several persons view the same screen, there is also sustained lateral bending of the neck. The relatively fixed position of the head, neck, and upper trunk is associated with symptom-producing neck muscle hypertonia and increased static postural traumatization of the articular surfaces of the cervical and upper thoracic vertebrae.

The remedy—aside from not viewing television—is to raise the television set so that the screen can be comfortably viewed by each person without assumption of this awkward sustained posture. Sometimes a chair with a lower or higher seat permits less strained posture.

Since television viewing in the home and elsewhere is likely to increase, physicians should be alert to recognize the syndrome of television neck and to prescribe proper treatment. Television equipment and furniture designers should be encouraged to develop home equipment that will make it possible for the viewer to enjoy television programs without maintaining strained posture for prolonged periods.

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A SIMPLE EVALUATION OF FOODS

To the Editor:—A question frequently asked, mostly by laymen, pertains to the relative value of different foods: "Are carrots a better food than potatoes?" "Do beets have much food value?" "How do spinach and kale compare in food value?" Obviously, if one were completely or largely on a potato diet, carrots in the diet would have a far greater value than an equal amount of potatoes. Yet conceivably there are diets that could not be improved by the addition of carrots.

It is realized that such questions have something in common with the question "Which is the more important, the hen or the egg?" The completely evasive, though inescapable, answer to the hen and egg question is that without one there cannot be the other. It is possible, however, to give a better answer in a comparative evaluation of different foods. The first requisite in such comparisons is to have representative analytical figures as to the content of the critical dietary essentials in any one food. Counting the essential amino acids, there are about 50 dietary essentials. Not all are critical in the sense that there is any danger of our not receiving an adequate supply, regardless of what our diet may be.

The Nutrition Board of the National Research Council, in setting up the recommended daily dietary allowances, gave recognition to what are commonly regarded as the critical dietary essentials. The recommended amounts naturally vary with the person, being affected primarily by age and activity and, to a lesser extent, by size and sex. For the purpose of the comparative evaluation of foods in the accompanying table the values for a 154 lb. (70 kg.) sedentary man and a moderately active 123 lb. (56 kg.) woman are used, since they are alike for most of the nutrients, and, in cases in which they differ, the median value has been used. These values are as follows: calories 2,400; protein 65 gm. (median, between 70 for the man and 60 for the woman); vitamin A 5,000 I. U.; thiamine 1.2 mg.; riboflavin 1.65 mg. (median between 1.8 for the man and 1.5 for the woman); niacin 12 mg.; and ascorbic acid 72.5 mg. (median between 75 for the man and 70 for the woman). It may be added that the use of these median values instead of the exact figure

Ratio of Daily Requirement of Nutrients to Daily Requirement of Calories in Foods *

	Protein (65 Gm.)	Ca (1,000 Mg.)	Fe (12 Mg.)	Vitamin A 5,000 I. U.)	Vitamin B_1 (1.2 Mg.)	Vitamin B_2 (1.65 Mg.)	Niacin (12 Mg.)	Vitamin C (72.5 Mg.)	Average
Canned Vegetables and Fruits									
Asparagus, white	3.1	1.8	8.8	1.2	4.9	4.2	6.9	24.0	6.9
Asparagus, green	3.5	2.1	16.8	12.0	6.6	6.7	8.1	24.0	10.0
Beans, baked	1.7	1.1	4.4	0.2	0.6	0.5	0.9	0.7	1.3
Beans, green cut	2.1	4.2	12.3	7.3	2.9	2.7	3.3	4.7	4.9
Beans, lima green	2.2	0.9	7.1	1.1	1.0	0.9	1.6	3.4	2.3
Beets, cubed	1.0	1.0	1.1	0.2	0.5	1.0	0.9	4.4	1.3
Carrots, cubed	0.9	2.1	5.0	208.5	1.6	1.0	0.3	2.1	27.7
Corn, white cream style	0.9	0.1	1.3	0.1	0.7	0.8	2.4	2.3	1.1
Corn, yellow cream style	0.9	0.1	1.3	0.7	0.7	0.8	2.0	2.2	1.1
Corn, white whole grain	1.0	0.2	1.4	0.1	0.6	0.9	2.6	2.5	1.2
Corn, yellow whole grain	1.0	0.1	1.1	1.0	0.7	0.9	2.2	2.3	1.2
Kraut	1.8	4.1	64.8	1.2	3.2	2.8	1.0	27.4	13.3
Mushrooms	5.7	0.8	5.3	0.4	1.7	14.7	16.9	3.9	6.2
Peas, Alaska	2.1	0.8	5.6	3.7	3.1	1.3	2.8	5.3	3.1
Peas, sweet	2.3	0.9	5.7	4.1	4.2	1.6	3.8	6.1	3.6
Pimentos	1.4	0.6	10.9	46.2	2.1	3.7	3.3	157.0	28.1
Peppers, sweet	0.9	0.6	11.5	51.4	2.5	3.8	4.5	124.3	24.9
Spinach	3.5	9.9	20.4	128.0	1.7	7.0	3.1	20.4	24.3
Sweet potatoes	0.5	0.5	1.1	43.2	1.0	0.6	0.9	4.9	6.6
Tomatoes	1.7	0.7	4.5	21.0	4.8	1.8	6.3	24.8	8.2
Turnip greens	2.9	12.9	4.9	113.2	1.6	7.0	6.2	34.8	22.9
Apricots, syrup	0.2	0.2	1.6	12.1	0.4	0.3	0.8	1.6	2.2
Blackberries, syrup	0.3	0.5	6.2	1.0	0.3	0.3	0.5	2.4	1.5
Blueberries, syrup	0.5	0.6	22.5	0.4	0.6	0.5	0.8	9.8	4.5
Cherries, red sour	0.6	0.5	10.5	7.8	1.0	0.4	0.7	3.9	3.2
Grapefruit segments	0.3	0.4	0.8	0.1	0.9	0.4	0.6	10.7	1.8
Peaches, cling	0.2	0.1	0.7	2.7	0.2	0.4	1.5	1.7	0.9
Peaches, Freestone	0.2	0.1	0.7	1.9	0.2	0.3	1.3	1.3	0.8
Pears, syrup	0.2	0.2	1.3	0.1	0.3	0.4	0.5	0.8	0.5
Pineapple, sliced	0.2	0.5	1.4	0.2	1.4	0.3	0.3	1.6	0.7
Plums, purple	0.2	0.2	2.2	6.3	0.5	0.3	0.8	0.6	1.4
Grapefruit juice	0.4	0.4	1.8	0.2	1.5	0.6	0.8	24.6	3.8
Orange juice	0.6	0.5	2.0	1.6	3.0	0.6	1.0	25.1	4.3
Pineapple juice	0.3	0.6	1.0	0.4	1.8	0.4	0.6	5.1	1.3
Tomato juice	1.5	0.8	8.6	19.9	5.3	2.0	7.4	23.6	8.6
Average	1.3	1.5	7.3	20.0	1.8	2.1	2.8	17.0	...
Canned Fish									
Mackerel	3.6	2.7	1.9	0.3	0.3	1.5	7.9	0	2.3
Salmon, pink	5.3	3.0	0.8	0.2	0.3	1.6	10.5	0	2.7
Sardines in oil	2.6	3.1	2.5	0.4	0.2	0.7	4.0	0	1.7
Sardines in tomato sauce	3.1	4.3	3.9	...	0.1	1.7	4.8	0	2.2
Shrimp, dry pack	8.2	2.1	5.8	0.3	0.2	0.4	3.7	0	2.6
Shrimp, wet pack	8.2	2.0	6.5	0.4	0.2	0.7	4.0	0	2.8
Tuna	3.5	0.1	0.9	0.1	0.3	0.8	8.0	0	1.7
Average	4.9	2.5	3.2	0.3	0.2	1.1	6.1	...	...
Noncanned Staple Foods									
Bread, white enriched	1.2	0.5	1.5	0	1.9	0.8	1.5	0	0.9
Milk, whole	1.9	4.1	0.2	1.1	1.2	3.5	0.2	0.4	1.7
Beef, cooked, all methods	2.9	0.1	2.3	0	0.5	0.8	3.7	0	1.3
Egg	2.2	0.8	3.4	3.4	1.4	3.1	0.1	0	1.8
Average	2.1	1.4	1.9	1.1	1.3	2.1	1.4	0.1	...

* Daily requirement is given in parentheses under each nutrient.

for a man or for a woman has no significant effect on the figures in the accompanying table.

The literal meaning of the figures may be illustrated with canned white asparagus, since it stands at the head of the list. It is not intended to suggest that any sedentary man or moderately active woman is ever going to eat enough white canned asparagus in a single day to provide the entire recommended daily requirement of 2,400 calories. But, if one supposes that this amount were consumed in one day, and it alone, 3.1 times the recommended protein would be supplied, 1.8 times the recommended calcium, 8.8 times the iron, 1.2 times the vitamin A, 4.9 times the thiamine, 4.6 times the riboflavin, 6.9 times the niacin, and 24 times the ascorbic acid (vitamin C).

In a similar manner, the meaning of the average figures at the bottom of the list of canned foods becomes clear. If the daily recommended calories were obtained by taking an equal number of calories from each of the 35 canned foods listed (a vegetarian diet), those canned foods would supply 1.3 times the recommended protein, 1.5 times the calcium, 7.3 times the iron, 20 times the vitamin A, 1.8 times the thiamine, 2.1 times the riboflavin, 2.8 times the niacin, and 17 times the ascorbic acid.

There is good reason for evaluating foods on the basis of the amount of the protein and noncalory nutrients supplied in proportion to the calories. Of all the factors for which the Nutrition Board has made recommendations, only calories are directly related to the amount of food consumed. If we eat less food than will supply our normal requirement of calories, we will lose weight; if we eat more, we will be burdened with overweight, and obesity is a major problem in nutrition. But no suggestion has ever been made of our getting harmful amounts of any of the other nutrients from our foods; the concern has been entirely with our getting the recommended amounts, and it has been intimated that greater amounts are all to the good.

The average figures in the last column of the table serve as rough comparative value of individual foods in their ability to supply critical nutrients; for example, 0.5 for pears as against 10.7 for green asparagus leaves little doubt about the comparative value of the two. But the figure 27.7 for carrots is largely due to the very high value (208.5) for vitamin A. All the other values for carrots, with the exception of that for calcium, being materially lower than for green asparagus.

The values for the canned foods have been calculated from the data in "Canned Foods in Human Nutrition" (Washington, D. C., National Canners Association, 1950). This represents the most comprehensive analytical survey of any class of food. Hundreds of samples from the entire country were collected, and the analyses were made in the nutrition departments of nine of our great universities. The values for the noncanned staple foods are from data in the U. S. Department of Agriculture Handbook no. 8, June, 1950.

Since the data in the table are based on chemical and microbiological technique they reveal nothing regarding availability. When there are data on availability, the figures in the table will assume far greater accuracy. It should also be remarked that nitrogen content is not a true measure of protein value; also, the high calcium content of spinach is known to be of little value nutritionally. In spite of these shortcomings some definite conclusions are evident. The vegetables as a group are outstanding in providing an abundance of all the critical nutrients in proportion to their calory value. They outrank the so-called staple foods and the fruits. As a class, fruits and vegetables supply vitamins A and C in great abundance. Since the ratio of vitamins A and C to calories is 20 and 17 for the canned vegetables and fruits, respectively, our vitamin A requirement would be met if they supplied but 5% of our calories and our vitamin C requirement would be met if they supplied 6% of our calories. While the data pertain more specifically to canned vegetables and fruits, they no doubt apply to other foods, irrespective of form.

E. F. KOHMAN
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CONTRIBUTION BY INDUSTRY TO MEDICAL EDUCATION

To the Editor:—The efforts to persuade industry of its share in the responsibility for the financial support of medical schools is well known to us all and is an endeavor of the greatest importance. This problem is so immediate and so vital that it tends to overshadow a second problem, of which I am writing you today.

The rapidly rising costs to the student in medical school have placed an extraordinarily heavy financial burden on each candidate, while at the same time the demands of the current-day curriculum make the time available for outside earnings insignificant for the most part. During this same time, as you well know, the income from scholarships and endowments has diminished. Were it not for the fact that the future of the medical school itself is at stake, this current dilemma of its students would assume much greater prominence.

Recently one of the pharmaceutical companies has recognized this as a special problem and has seen fit to give to every approved medical school in the country $1,000 to be disbursed to students in need. This action by a pharmaceutical company seems to me to deserve recognition by the members of the American Medical Association, who are so interested in seeing problems solved through the efforts of private enterprise.

If the board of trustees of such companies as the Charles Pfizer Company, which made the above-mentioned donation, can be encouraged by appropriate recognition to increase and to generalize their donations to medical education they could provide a large part of the total needs of the medical schools. Although $70,000 is not large in terms of the total need, it does seem to indicate a recognition by a pharmaceutical company of a direct responsibility for the needs of medical education. It would be regrettable if this sense of responsibility were not encouraged.

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CHICAGO MEDICAL BOOK COMPANY

To the Editor:—We wish to inform your readers that the Chicago Medical Book Company has had nothing to do with nor did we know anything about the printing, publication, or distribution of a pamphlet, "The Hospital Superintendent: What Makes Him Tick?" This is reported to be a study in human behavior, but it is unsigned, and there appears to be no way of identifying the author or sponsor. Unfortunately, at the end of the document appears this statement: "Additional copies of this book may be obtained from the Chicago Medical Book Co., Jackson and Honore Streets, Chicago, Illinois."

The Chicago Medical Book Company has never been contacted by any person or persons requesting the use of our name with regard to this book or a book of this nature, nor have we ever given our permission to any person or persons allowing them the use of our name for the sale, distribution, or procurement of this book. We are completely ignorant as to what person or persons would use our company's name on the last page of this book as a source of supply. Until the post office called us about postage due on 120 of the booklets, we knew nothing whatever about it. We have had many requests, emanating from various sections of the United States, requesting additional copies of this booklet.

We are most desirous of correcting this unfortunate incident and take this opportunity to inform your readers of the above facts. In the event that they have any information regarding this publication, we would be more than happy to be advised of the same.

A. C. BOWERS
Advertising Manager
Chicago Medical Book Company
Jackson and Honore Streets
Chicago 12.

MISCELLANY

MEDICAL LIBRARY OF A NON-UNIVERSITY GENERAL HOSPITAL

A Five-Year Progress Report on the Medical Library of the New Britain General Hospital

Paul D. Rosahn, M.D.
and
Sadie M. Karpman, New Britain, Conn.

The New Britain General Hospital is a general, nonprofit association hospital of 267 beds. It is the only hospital of its type in an industrial community that, with its suburbs, has a population of approximately 100,000. The active, courtesy, and general practice staffs consist of 84 physicians, of whom 35 have been certified by various specialty boards. An approved residency training program is conducted in surgery, gynecology, obstetrics, internal medicine, and pathology.

The Hospital Medical Library was reorganized in 1946, pending completion of its present quarters, which it occupied in June, 1947. The area presently assigned to the library consists of a main reading room with tables and chairs accommodating about 15 persons, an adjacent stack room, and a nurses' reading room, located in the dormitory of the School of Nursing. An earlier report [1] outlined the developmental background of the library and discussed the guiding principles under which it operates. During the past five years there has been ample opportunity to test the original thinking on the organization and administration of the library against actual experience. Many ideas have been altered and revised in the light of this experience, and new thoughts have been incorporated in the program. The present five-year progress report has been prepared in the hope that it may be helpful to other non-university hospital groups interested in establishing a medical library in their institutions.

THE LIBRARY COMMITTEE

From its inception, the professional supervision and control of the library has been vested in a committee of the medical and nursing staffs. This committee, appointed by the board of directors of the hospital, is directly responsible to the board. The library is a recognized department of the hospital, and the librarian, as a hospital department head, is administratively responsible to the managing director.

The library committee [2] is composed of five members, two of whom, the director of nursing service and the school of nursing and the pathologist, are full-time hospital employees. The other three members, selected from the active medical staff, are each appointed for staggered three-year terms. Regular meetings of the committee are held each month, the librarian acting as secretary. Minutes of the meeting are recorded, and copies are distributed to each member of the committee, to the managing director, and to the librarian. Special meetings to consider urgent problems may be called by the chairman of the committee. The appointment to the library committee of the director of nursing service and the school of nursing is in accord with the originally stated policy of combining the library of the School of Nursing with the medical library.

Each member of the committee has recognized the great responsibilities of his office, and rarely does a member fail to attend the scheduled meetings. These are largely concerned with reviewing suggestions presented in writing by members of the medical staff for the purchase of textbooks or journals and acting on these recommendations. Such decisions are usually based on the general usefulness of the textbook or journal to a staff of varied interests and specialty training and always with the keen awareness of a relatively limited budget. In actual practice, the total annual budget is determined by the managing director, but the distribution and allocation of funds within the budget rest largely on the recommendations of the library committee. Other matters under discussion are such items as coverage during the librarian's vacations and other absences, the purchase of additional book shelves and large equipment, methods for increasing the usefulness of our facilities to the professional staff, and continuing thinking on ways and means of enhancing the attractiveness of the library quarters. The library committee has disapproved the use of the library reading room for small meetings or classes. The library committee believes that these activities would deprive members of our professional staff of the use of the library facilities during the meetings and would thus defeat a primary objective of the library, namely, round-the-clock accessibility.

FINANCES

Since a hospital library is a nonincome producing unit of the institution, its financial support must be derived from endowments, from contributions, or from general funds. Originally it was hoped that our library would be at least partially sponsored by specific bequests, but this hope has not been realized and we have had to depend on the other two sources to secure our operating funds. The members of the medical staff, at the inception of the program, in 1946, unanimously approved a self-imposed library tax of $15 each per annum, and without dereliction this amount has been subscribed each year. The treasurer of the staff transfers these library dues to the hospital, which ear-marks them for library use. In addition, small library fees paid by student nurses are allocated to the library fund. These monies comprise less than one-fourth of our total annual expenditures, the remainder being provided by the board of directors from other sources. The action of our directors in so generously supporting a hospital activity that is all too frequently by-passed or ignored is a tribute to their deep interest in developing and maintaining high medical standards.

New Britain General Hospital Library
Original Budget, Actual Expenditures from 1946 Through 1951 and Anticipated Budget for 1952

	Journals	Binding	Text-books	Miscellaneous and Salaries	Total
Original Budget	$1,000.00	$1,000.00	$500.00	$2,500.00	$5,000.00
Actual Expenditures					
Nov., 1946-Sept., 1947	999.43	397.32	601.90	2,438.54	4,437.19
Oct., 1947-Sept., 1948	969.99	487.61	537.50	3,033.38	5,028.48
Oct., 1948-Sept., 1949	1,081.81	264.86	227.15	3,048.76	4,622.58
Oct., 1949-Sept., 1950	1,210.79	756.55	168.47	3,361.99	5,497.80
Oct., 1950-Sept., 1951	1,181.42	543.42	375.26	3,547.63	5,647.73
Anticipated Budget, 1951-1952	$1,200.00	$ 550.00	$500.00	$3,897.00	$6,147.00

LIBRARY BUDGET

Actual experience has produced two significant changes in our original tentative annual budget, as shown in the table. We overestimated the cost of binding our journals—all our journals are permanently bound promptly on the completion of a volume—and we did not foresee the general inflationary trends that would require upward adjustment of the salary paid to our full-time librarian. In spite of these developments, the total expenditure for the five-year period exceeded the anticipated operating expenses of $25,000 by only $233.78. Approximately 25% of the total was derived from staff dues and nurses' library fees. During the current fiscal year, the hospital will spend out of general funds about $5,000 for library purposes.

LIBRARY CONTENT AND SERVICES

The conviction of the original library committee that the library should concentrate on journals rather than on textbooks has been reaffirmed not only by newly appointed members of the committee but also by staff approval. We are now receiving 126 periodicals, of which 6 are gifts to the library. Represented among our journals, in addition to the recognized

Pathologist (Dr. Rosahn) and Medical Librarian (Mrs. Karpman), New Britain General Hospital.

1. Rosahn, P. D., and Olmstead, M. V. O.: The Medical Library of the New Britain General Hospital, Connecticut M. J. **12**: 23, 1948.

2. The following persons have served on the library committee: Dr. H. Bellach, Dr. A. J. Canzonetti, Miss A. E. Mooth, R.N., Dr. P. D. Rosahn, Dr. D. E. Wilson, Miss V. Duxbury, R.N., Dr. H. M. Clarke, and Dr. V. J. Squillacote. The first five listed here constitute the library committee at this writing.

periodicals covering the various clinical specialties of medicine, nursing, and dentistry, and also of hospital administration, are many others in the various basic sciences. An attempt has been made to supplement our journals with accredited textbooks covering the different medical specialties, but preference has consistently been given to journals. Accessions for the year ending Sept. 30, 1951, comprised 199 bound volumes of periodicals and 52 textbooks. Our inventory on this date included 1,677 bound volumes of periodicals and 1,239 textbooks. All our journals now have running files of bound volumes dating back for a minimum of five years.

The books and journals in our own library have been supplemented by interlibrary loan material borrowed from many generously cooperating organizations. Among these are the Yale Medical Library, the American Medical Association, the Armed Forces Medical Library, the Hartford Medical Society Library, and the New Britain Institute Library. In the year ending Sept. 30, 1950, for example, the following interlibrary loans were made: 91 bound journals, 52 current periodicals, 13 textbooks, 84 films and slides, 10 pamphlets, 2 microfilms, and 4 photostats and 12 paintings for display on the library walls.

All the libraries mentioned have been extremely helpful in supplying us with material not in our inventory, but special mention should be made of the Yale Medical Library, our principal source of interlibrary loan matter. We early profited by the counsel of the librarian and staff of that great institution, and they have continued to provide us generously with help and guidance. Through our institutional annual contribution to the Associates of the Yale Medical Library, we have attempted to give tangible if modest expression of our appreciation for the interlibrary loan service that the Yale Medical Library has given us.

CLASSIFICATION SYSTEM

It has been our experience that current periodicals, bound or unbound, are easily located on the shelves when arranged in alphabetical order according to the first important word of the title. We have not found it necessary to classify journals according to subject, but this can easily be done in the future if expediency demands such a classification.

At the time of organization of the library, all the major classification systems were reviewed in order that we might determine which would most suit our requirements. These systems have their individual merits, but it was decided that the Cunningham System was the best for our needs, and it was therefore adopted. Subsequent experience has indicated that the Cunningham System, because of its elasticity and simplicity, is ideally designed for a library of our size and type.

ATTENDANCE AND CIRCULATION

The value of a library is not in the amount and variety of material it contains, in the spaciousness of its quarters, or in the cost of its maintenance, but rather in the use to which it is put. Our library has become the foundation on which a vigorous residency training program has been built. Moreover, it has provided a stimulus to our medical and nursing staffs in their desire to maintain familiarity with the current literature. During the 1950-1951 fiscal years there were 867 recorded visits by members of the medical staff, 784 visits by nursing personnel, and 666 visits by others. In addition, there was an unknown number of visits by persons who did not sign our visitors' daily record. In the same year, the following items were borrowed: 421 current periodicals, 169 bound journals, and 657 textbooks. These visits and loans were without doubt important factors in maintaining high medical standards in the hospital.

But more specific benefits accrued to those of our medical staff who were preparing for specialty board examinations. Twelve members of our resident and general staff successfully took these examinations within the past three years. All of them prepared for the ordeal with the help of material in our own library and through our interlibrary loan arrangements. In no instance was it necessary for these physicians and surgeons to spend valuable time and energy traveling to distant places for their library needs.

In the earlier report already mentioned, it was indicated that there are extant two basic conflicting attitudes in library policy. With rigid custodial supervision, and restricted circulation of textbooks and journals for outside reading, a minimum of losses may be expected to accrue. On the other hand, where custodial care is only incidental, and where free withdrawal of library material is permitted and encouraged, the library content receives wide circulation, but losses of many items may be anticipated. The library committee was of the opinion that it was more desirable to have wide circulation with its accompanying probable losses than to have limited circulation and no losses. Accordingly, a liberal policy was adopted, by which access to the library was permitted every day round the clock, even in the absence of the librarian, and at all times library material other than reference books and encyclopedias could be withdrawn. This policy has been happily rewarded, for we have incurred no losses during our five years of operation.

COMMUNITY SERVICE

The only medical library in the city of New Britain is located at the General Hospital. Since many professional persons active in the community in medical and allied fields do not have hospital appointments, it was early decided to invite them to use the facilities of the hospital library. Retired physicians, city-employed physicians, industrial physicians, dentists, nurses, and the faculty and students of the State Teachers College have been encouraged to use the resources of our library. This doctrine of a community medical library, organized and maintained at the local community hospital, is another example of the many services other than the care of the hospitalized sick that a hospital can render to the community in which it is located.

MEDICAL LIBRARY POLICIES

The following library policies are being pursued at this writing:

1. The medical library consists of a main library and a library annex. The main library is located in the basement of the main hospital building and consists of a reading room and stack room, with additional storage space across the hall from the main quarters. General reference books, medical journals and books, and bound or unbound periodicals to be issued on a loan basis are housed in the main library. The library annex is located in the nurses' residence and comprises reference volumes and other material that may not be borrowed. The annex also provides space for storing bound journals dating back more than 10 years.

2. The main library is intended for use by all professional personnel connected with the hospital. This includes physicians, dentists, nurses, dietitians, physical therapists, technicians, and social workers. Members of these professional groups in the community, not officially connected with the hospital, are also invited to use the library facilities, with loans made at the discretion of the librarian.

3. The library annex is for the convenience of the nursing staff. It is unsupervised and is open at all times.

4. The main library is open and the librarian is on duty on Monday through Friday from 8 a. m. to 4:30 p. m. and on Saturday from 8 a. m. to 12 noon. It is closed on Sundays and on all legal holidays officially observed by the hospital. During the hours when the main library is officially open, it may be used both as a reading room and for the issuance of loan material.

5. During the hours when the library is officially closed, the key may be obtained from the admitting office if signed for and returned promptly after the user leaves the library.

6. All books and periodicals taken from the main library must be charged. When the librarian is off duty, a self-charging system is permitted. The borrower fills out a loan slip and drops it into the depository provided.

7. With the exceptions noted below, books and bound periodicals may be borrowed for two weeks and may be renewed for another two weeks, provided they have not been requested by another reader. If, during the period of renewal, they are requested by another reader, they are subject to recall at once. If a volume that is on loan is needed for a reserved shelf, it may be recalled before the limit of the loan period. The latest bound volume of a journal may be borrowed for one week only.

8. Reference books, such as systems of medicine and surgery, bibliographies, indexes, dictionaries, encyclopedias, current periodicals (latest issue received), and books on the "new book table" may not be taken from the library under any circumstances.

9. Unbound periodicals, books reserved for special courses, and reference books (except those restricted under paragraph 8) may be borrowed for overnight use only, i. e., after 4 p. m. Monday through Friday and after 11 a. m. Saturday. They must be returned to the library by 10 a. m. the following morning. Such material taken out Saturday must be returned by 10 a. m. Monday. When the library is officially closed, one may return books and periodicals by using the drop boxes provided in the staff room and at the main library entrance.

10. If a book or journal is lost, the borrower will be taxed the cost of replacement.

PERIODICAL SUBSCRIPTION LIST

Much thought was originally given to the selection of journals. Any newly published journal is reviewed by the library committee, which decides whether or not to add it to our subscription list.

THE HOSPITAL MEDICAL LIBRARY

A library is a living organism. To survive it must be generously nurtured, carefully guided, and constantly tended. A library consisting of randomly selected books and journals, housed on a few dusty shelves, in inaccessible, cheerless quarters, an undeveloped, unused and uninspiring library, is a dead library. A quiet and respectful interment, as befits the honored dead, should be its generous reward. A library proudly supervised, judiciously enlarged through carefully chosen acquisitions, groomed, culled and cultivated, is a living library. Such a library provides knowledge and sustenance to those who seek its haven.

How can the average hospital acquire such a library? Money is necessary, yes. Money provided by the staff, by nurses, and by the administration. But above and beyond the need for money, there must be the deep conviction by medical staff and by administration, that no other single use of funds will so measurably improve the medical standards of the institution. Such a conviction does not arise *de novo*. One or more dedicated souls, members of the staff, must, by discussion, persuasion, exhortation, and conciliation, strive to engender this concept in both staff and administration. Once this has been accomplished, the library is secure.

92 Grand St.

MEDICAL MOTION PICTURES

Journey to Reality: (PMF 5116C) 16 mm., black and white, sound, showing time 40 minutes. Produced in 1951 by the United States Army. Procurable on loan from Area Surgeon of the Army Area in which the request originates.

This film points out the value of prescribed occupational therapy and shows the need for cooperative efforts between psychiatrists and occupational therapists as well as other ward personnel. A number of condensed case histories are given and the various therapeutic approaches illustrated by excerpts from the patient's daily activity. For example, the overactive manic patient is put at a loom, which allows her to expend considerable energy along useful channels; the hostile patient is encouraged to "make his own choice" in the metal shop, where he can work off feelings by pounding; the retarded and depressed patients are given simpler, less taxing activities.

A more descriptive title for this film might possibly have been "The Beginning of the Journey to Reality," since the span of the patients' total program is presented briefly, both in terms of time and of things to be done. Some of the case history portrayal is a bit strained and unrealistic. The medical aspects of the program are well presented. The photography and narration are well done. Its greatest usefulness would be for the orientation of hospital personnel generally and in particular occupational and physical therapists and psychiatric social workers. It could also be used in beginning courses for occupational therapists. Physicians interested in psychiatric problems would also be interested in this film.

BUREAU OF LEGAL MEDICINE AND LEGISLATION

MEDICOLEGAL ABSTRACTS

Charitable Hospitals: Liability for Burns to Child of Pay Patient.—The plaintiff, an infant, filed suit for damages for burns alleged to have been caused by the negligence of the servants of the defendant hospital. The plaintiff was placed in a bassinet immediately after her birth, and a hot water bottle was also placed therein to keep her warm. About two hours later, after removal to the nursery, she was found to have burns on her head and body. The defendant hospital made a motion for a summary judgment in its behalf on the ground that it was a charitable hospital and therefore free from liability in this case. The motion was heard by the superior court, Newcastle, Del.

The question of whether a nonstock, nonprofit, charitable corporation, which conducts and maintains a hospital by public and private contributions and funds received from those who are able to pay, is liable for injury to a patient caused by the negligence of its agents and employees, such as nurses, has never been decided in this state, said the court. It is an important question, and many decisions have been rendered on it by the various courts throughout the country. These decisions are not only conflicting but many of them are also accompanied by dissenting opinions. After discussing the history of the liability and nonliability of charitable institutions from 1846 to the present time and after citing numerous cases considering this question, the court quoted from section 294 of Harper on "The Law of Torts" as follows: "The immunity of charitable corporations in tort is based upon very dubious grounds. It would seem that a sound social policy ought, in fact, to require such organizations to make just compensation for harm legally caused by their activities under the same circumstances as individuals before they carry on their charitable activities. The policy of the law requiring individuals to be just before generous seems equally applicable to charitable corporations. To require an injured individual to forego compensation for harm, when he is otherwise entitled thereto, because the injury was committed by the servants of a charity is to require him to make an unreasonable contribution to the charity, against his will, and a rule of law imposing such burdens cannot be regarded as socially desirable nor consistent with sound policy."

It is contended, said the court, that the overwhelming weight of authority in the United States is in favor of the exemption of charitable corporations from liability for the torts of their agents and employees. After reading many cases decided in the various states throughout the country, the court was convinced that the contention is, at least, doubtful. The numerous distinctions made in the decisions certainly weaken their effect. There is quite a difference, the court continued, between charitable institutions today and those that existed when they were first held to be exempt from tort liability. Those that existed at that time were small and the funds that they had were not large when compared with many that we find today, the funds of which are provided for by foundations and in some instances are unlimited. The argument made in some of the earlier cases, that the funds of the institution would soon become exhausted or that persons would not make donations for charitable purposes if they were used to pay damages does not apply with the same force as it did at that time. There can be no doubt that the trend of decisions today and the views expressed in many of the law journals is in favor of imposing full liability on charitable corporations for the torts of their agents and employees.

Continuing, the court said that it was convinced that the general principle that makes every person responsible for his own legally careless action should apply with equal force to charitable corporations. The doctrine of *respondeat superior* also applies to charitable corporations and makes them responsible for the

negligent acts of their agents and employees, when such acts are clearly incidental to the business of the corporation, to the same extent that individuals are. This is true whether or not the beneficiary pays for the service that he receives. It is unreasonable to hold that persons who do not pay for the service that they receive from a charitable corporation cannot recover for injury resulting from the negligent acts of those for whose acts the corporation is responsible when such acts are incidental to the business of the corporation. The court, therefore, held that whether the defendant was negligent by failing to provide proper equipment in the delivery room or nursery of his hospital or whether the agents or employees of the defendant were negligent by failing to properly care for the plaintiff were questions of fact for the jury, but it denied the defendant's motion for summary judgment. *Durney v. St. Francis Hospital, 83 A. (2d) 753 (Delaware, 1951).*

Ethics: Sale of Dental Practice by Widow for Share in Future Earnings.—The plaintiff sued to recover sums paid under a conditional sales contract covering the sale of a dental practice. From a judgment in favor of the defendant, the plaintiff appealed to the Supreme Court of Washington.

The defendant was the widow and executrix of the estate of a deceased dentist and as such became owner of the equipment, accounts receivable, lease, and going business of what was known as "Dr. Conway's Dental Clinic." She entered into a contract for the sale of this asset to the plaintiff dentist. The purchase price was to be $300 a month for ten years, a total of $36,000. In addition, and specifically as payment for the "going business," the defendant was to receive a share of the net profits for the first five years, her percentages to be 70% for the first year, 60% for the second year, and 55% for the following three years. Before any profits were to be divided, however, $300 was to be paid on the purchase price, and the plaintiff was to draw $750 each month, in addition to the payment of all other operating expenses. The plaintiff was taking over an established dental practice with no down payment. The contract with the plaintiff further provided that the defendant would ". . . of necessity dedicate a considerable portion of her time to the protection of her security and advancement of the interest of the business in order that it may return to her the amount contemplated by the parties as purchase price under all of the circumstances now existing." Implementing the above was paragraph 7 providing: "It is further agreed that the doctor shall spend his whole time to the professional care of the office and shall have exclusive control over professional conduct and practice in said office and that the seller shall have the right to be the manager of said business and shall have the right to superintend the business management of the office." Title to fixtures and equipment was reserved to the defendant to secure the payments provided for by the contract; the lease was to be renewed in her name until payment under the contract was complete, at which time it was to become the property of the plaintiff. All new accounts receivable were to be assigned to the defendant during the first five years "as security only."

After the contract had been in force about six months, the plaintiff notified the defendant that the contract was illegal as far as it provided for her participation in the business in any way, and any sums that it was contemplated that the defendant should receive therefor would be illegal. The notice also stated that the books of the clinic would no longer be open to the defendant's inspection or approval and that the defendant was to remain away from the clinic and the employees except for reasonable inspection. In conclusion, the notice said that in the plaintiff's opinion the contract was principally a legal one and that the illegal portions, which contemplated paying the defendant a percentage for management, could be deleted and the management cancelled, but the balance of the contract continued in force.

The Supreme Court said that it could find nothing in the contract to the effect that the percentage payments to the defendant were to be compensation for her management. The contract definitely stated that the percentage of profits she was to receive was "payment for the going business herein contracted to be sold." There was nothing unlawful in the defendant's ownership of the property and interests that she sold to the plaintiff, although, under state law and under decisions of the Washington Supreme Court, the defendant could not have employed anyone to take over her husband's practice and operate it for her. It can not be gainsaid that she had the right to sell that which she owned, either for cash or on terms, and, if on terms, she had the right to protect her interests in any way consistent with the public policy of the state. We have carefully examined the contract, the court continued, and as far as we can determine, it is a bona fide contract of sale calculated to protect and to benefit both parties, and none of the provisions of that contract brand it illegal or contrary to public policy. The fact that the defendant was to have a relatively large percentage of the net profits during the first five years does not establish that she owns, maintains, or operates an office for the practice of dentistry, but rather that she and the plaintiff had agreed on a formula for arriving at a value of the "going business," which we conceive to be the good will of the established dental practice.

The two provisions of the contract that gave the plaintiff great concern are the ones granting the defendant (a) a percentage of the profits and (b) the right to be the business manager and to superintend the business management of the office. It is common knowledge, said the Supreme Court, that many physicians and dentists, and certainly most clinics, leave the details of business records, the issuing of statements, the collection of accounts, and the details of disbursements for supplies and equipment to personnel employed for that purpose, and we do not regard the handling of those details as constituting the practice of medicine or dentistry, although their capable performance may be essential to make that practice profitable. The fact that the same details are supervised by one who, instead of being an employee, is selling the practice under a conditional sales contract does not of necessity constitute such ownership, maintenance, or operation of an office for the practice of medicine or dentistry as is contemplated by the statute, although it could well be a factor requiring a closer scrutiny of the entire transaction to determine whether it is actually what it purports to be or, instead, is a scheme to subterfuge to violate the law. If the plaintiff is entitled to any relief, it is not because the contract is illegal, but because the defendant has exercised a control over the business that constitutes, in fact, the management and operation of a dental office. Some of the conduct complained of by the plaintiff might well be within her rights under the provisions of the contract that were designed for her protection, but, concluded the Supreme Court, the allegations that she "effectuated her control and management of said business by maintaining control of the finances, control of the books, control of the patients, and control over appointments of patients . . .," if true, clearly entitles the plaintiff to relief of some sort.

The plaintiff also contended that the defendant could receive no percentage of the profits, that so long as he paid her $300 a month he was complying with all the legal provisions of their contract, and that he could deny her even an examination of the books. It must be borne in mind, said the court, that the plaintiff did not allege or even suggest that this was not a bona fide sale or that the sale was being used as a blind or pretext to enable the defendant to practice dentistry in contravention of the statute. We are in entire accord with the trial court that the plaintiff cannot recover on the theory that a portion of the contract is illegal. Plaintiff's recovery, if any, must be on the theory that the defendant's conduct so breached the contract as to warrant his abandonment of it, to his damage.

The Supreme Court, therefore, felt that the defendant's demurrer should have been overruled and the plaintiff afforded an opportunity to prove his allegations. The judgment of the trial court in favor of the defendant was accordingly reversed and the cause remanded to the trial court for further hearing. *Prichard v. Conway, 234 P. (2d) 872 (Washington 1951).*

MEDICAL LITERATURE ABSTRACTS

UNITED STATES

A.M.A. Arch. Internal Medicine, Chicago

89:523-688 (April) 1952

*Control of Hypertension by Hexamethonium and *l*-Hydrazinophthalazine: Preliminary Observations. H. A. Schroeder.—p. 523.

*Histoplasmosis in Epidemic Form: Follow-Up Study. B. Schwartz and L. J. Spitz.—p. 541.

Mental Changes Associated with Hyperparathyroidism: Report of Two Cases. T. E. Fitz and B. L. Hallman.—p. 547.

Physical Medicine and Rehabilitation in Acute Myocardial Infarction. L. B. Newman, M. F. Andrews, M. O. Koblish and L. A. Baker. —p. 552.

Heatstroke in Parkinsonism. R. E. Litman.—p. 562.

Benign Bundle Branch Block. J. P. Vazifdar and S. A. Levine.—p. 568.

*Leptospiral Meningitis. P. B. Beeson and D. D. Hankey.—p. 575.

Effect of Therapy on Blood Volume, Blood Pressure, and Spleen Size in Polycythemia Vera. T. C. Prentice, N. I. Berlin and J. H. Lawrence. —p. 584.

l-Arterenol (Levophed®) in Treatment of Shock Due to Acute Myocardial Infarction. A. J. Miller and L. A. Baker.—p. 591.

Whipple's Disease: Review of Literature and Report of Two Cases. F. R. Russo.—p. 600.

Rationale and Clinical Use of Steroid Hormones in Cancer. S. I. Griboff. —p. 635.

Hexamethonium and *l*-Hydrazinophthalazine in Hypertension.—An antihypertensive drug of only moderate potency, *l*-hydrazinophthalazine, was found to be considerably more effective in patients who had undergone sympathectomy. Malignant hypertension was also found to be susceptible to its action. This suggested that "medical sympathectomy," induced by sympatholytic or ganglionic blocking agents, might enhance the antihypertensive action of *l*-hydrazinophthalazine. It was decided to combine its use with that of a soluble, apparently innocuous ganglionic blocking agent, hexamethonium chloride. Forty patients with chronic arterial hypertension severe enough to require hospitalization, and resistant to dietary measures, thiocyanate administration, surgical measures, and psychotherapeutic procedures were treated. Hexamethonium chloride was usually given in initial doses of 125 to 250 mg. every eight hours, which were increased daily until a maximum of 500 mg. every four hours was reached, or blood pressure showed wide fluctuations, reaching normal levels. At this point *l*-hydrazinophthalazine was added in doses of 25 to 50 mg. every eight hours, in amounts increased by daily increments until a dose of 100 mg. every four hours was reached or the blood pressure had become normal. After normal blood pressure had been achieved in the hospital, a member of the patient's family was instructed in measuring blood pressure; a schedule was arranged for use of the drugs at home, and the patient was discharged. Patients with "benign" arterial hypertension achieved normal or nearly normal blood pressure in every case. Continuous administration was essential for control. In some cases "malignant" hypertension was well controlled with oral doses, while in others it was only partially controlled. The malignant stage was altered favorably in all but two. The method was practical for use at home in intelligent patients. It represents a way of controlling hypertension, but it is not a "cure." Long-term results cannot be evaluated until more time has elapsed. Subsequent experience with 60 patients who have been taking these drugs for from 10 to 28 weeks has shown that 30 have maintained normal blood pressure levels. Of 22 in the malignant stage, 8 have normal blood pressure and 12 slight hypertension; the malignant stage has regressed in all instances. Tolerance to the drugs has not appeared.

Epidemic Histoplasmosis: Follow-up Study.—Histoplasmosis in its acute form occurs either as a benign or as a fulminating fatal disease. It usually appears sporadically, but this paper reports follow-up observations in 1 of 26 cases of diffuse pneumonitis that occurred as an epidemic at an Army camp in 1944 and were reported as cases of "an unusual pulmonary disease." The acute stage of the disease lasted one week. At this time roentgenographic inspection revealed a diffuse mottling throughout both lung fields. No tubercle bacilli were found, and the Mantoux test gave a negative reaction. The coccidioidin skin test likewise gave a negative reaction. Agglutination tests for brucellosis, tularemia, and typhoid and serologic tests for psittacosis all gave negative results. The reactions to serologic tests for histoplasmosis were also negative. A physical examination of one patient six years later showed no abnormality, but roentgenograms of the chest revealed shadows suggestive of the end-stage of pulmonary histoplasmosis. A skin test with histoplasmin gave a strongly positive reaction (4+), while reactions to coccidioidin and Mantoux tests were negative. A complement-fixation test for histoplasmosis, using the yeast phase antigen of Histoplasma capsulatum, was positive to a titer of 1:140 and negative for other fungi. Observations on this patient suggest that the other members of the group thought to have an unusual pulmonary disease also had a benign form of pulmonary histoplasmosis. The authors mention four similar epidemics, the cause of which has never been established. It is hoped that this report will stimulate further follow-up study in these cases.

Leptospiral Meningitis.—Only three strains of Leptospira (Lept. icterohemorrhagiae, Lept. canicola, and Lept. pomona) have been identified here. Although cases of Weil's disease (spirochetal jaundice) have been recognized in various parts of the country, there is reason to believe that the incidence of leptospiral infection is probably greater than is appreciated. The authors searched for evidence of leptospirosis in patients with "benign aseptic meningitis." Positive results were obtained in 6 of 35 patients admitted to one Atlanta hospital during a two year period. A seventh patient was observed in another Atlanta hospital during the same period. Serologic tests for evidence of leptospiral infection were made on approximately 500 pairs of serums obtained from other localities in the United States. These had been submitted to other laboratories for serologic tests for neurotropic viral infection. It was known, however, that many of them had been collected during epidemics of mumps, poliomyelitis, and encephalitis. Leptospiral agglutinins in titers of probable significance were found in 17 instances. Data on these 24 patients permit the following statements: 1. Leptospiral meningitis occurs in many parts of the United States. 2. The clinical features resemble those of meningitides of viral origin, such as mumps, lymphocytic choriomeningitis, and nonparalytic poliomyelitis. 3. Ten of the 24 cases occurred in the month of August. 4. The disease is commoner in males below the age of 30. Laboratory procedures for the diagnosis of leptospiral infection are described.

American Journal of Public Health, New York

42:353-498 (April) 1952. **Partial Index**

Emergency Sanitation Lessons from the 1951 Flood in Kansas. D. F. Metzler.—p. 364.

Principles of Emergency Feeding for a Large Metropolitan Area in Catastrophe. R. S. Goodhart and N. Jolliffe.—p. 373.

Membrane Filter in Water Quality Tests. H. F. Clark and P. W. Kabler. —p. 385.

Use of Differential Media with Membrane Filter. P. W. Kabler and H. F. Clark.—p. 390.

Immunization of Adults Against Diphtheria and Tetanus. G. Edsall. —p. 393.

Lead Poisoning: Case Finding Program. J. E. Smith, B. W. Lewis and H. S. Wilson.—p. 417.

Evaluation of "Breast Self-Examination" Film. E. M. Cohart and J. K. Hill.—p. 430.

Periodicals on file in the Library of the American Medical Association may be borrowed by members of the Association or its student organization and by individual subscribers, provided they reside in continental United States or Canada. Requests for periodicals should be addressed "Library, American Medical Association." Periodical files cover only the last 11 years, and no photoduplication services are available. No charge is made to members, but the fee for other borrowers is 15 cents in stamps for each item. Only three periodicals may be borrowed at one time, and they must not be kept longer than five days. Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted.

American Review of Tuberculosis, New York

65:357-504 (April) 1952

Chemotherapy of Experimental Tuberculosis: V. Isonicotinic Acid Hydrazide (Nydrazid) and Related Compounds. J. Bernstein, W. A. Lott, B. A. Steinberg and H. L. Yale.—p. 357.
*Antituberculous Properties of Hydrazines of Isonicotinic Acid (Rimifon, Marsilid). W. Steenken Jr. and E. Wolinsky.—p. 365.
Pharmacologic and Toxicologic Observations on Hydrazine Derivatives of Isonicotinic Acid (Rimifon, Marsilid). W. M. Benson, P. L. Stefko and M. D. Roe.—p. 376.
Pharmacology of Isonicotinic Acid Hydrazide (Nydrazid). B. Rubin, G. L. Hassert Jr., B. G. H. Thomas and J. C. Burke.—p. 392.
Hydrazine Derivatives of Isonicotinic Acid (Rimifon, Marsilid) in Treatment of Active Progressive Caseous-Pneumonic Tuberculosis: Preliminary Report. E. H. Robitzek and I. J. Selikoff.—p. 402.
Absorption, Distribution, Excretion, and Short-Term Toxicity of Isonicotinic Acid Hydrazide (Nydrazid) in Man. D. F. Elmendorf Jr., W. U. Cawthon, C. Muschenheim and W. McDermott.—p. 429.
Observations on Electrocardiogram in Surgically Treated Pulmonary Tuberculosis. V. O. Hertzman and A. K. Mathisen.—p. 443.
Prevalence of Previously Unknown Tuberculosis in Persons Not Participating in Mass Chest Roentgenographic Surveys. W. T. Palchanis.—p. 451.
Traction Diverticula of Esophagus in Middle Lobe Syndrome. H. L. Katz.—p. 455.
Spirometric Studies in Pneumoperitoneum. G. C. Leiner and S. Abramowitz.—p. 465.
Correlation of Biologic Properties of Strains of Mycobacterium with Their Infrared Spectrums: II. Differentiation of Two Strains, H37Rv and H37Ra, of M. Tuberculosis by Means of Their Infrared Spectrums. H. M. Randall, D. W. Smith and W. J. Nungester.—p. 477.

Antituberculous Properties of Hydrazines of Isonicotinic Acid.—Preliminary observations on two hydrazines of isonicotinic acid ("rimifon" and its isopropyl derivative, "marsilid") indicate that they have tuberculostatic and tuberculocidal action in vitro and a beneficial effect on animals infected experimentally. Parenteral administration of 10 mg. of "marsilid" twice daily (approximately 35 mg. per kilogram of body weight daily) was tolerated well by guinea pigs for 60 days; up to 35 mg. per kilogram daily of "rimifon" was tolerated well for six weeks. Tolerance tests for oral administration to guinea pigs showed that doses up to 40 mg. per kilogram daily of both "marsilid" and "rimifon" were tolerated well for two weeks. Intramuscular tests with rabbits showed good tolerance for 70 days with doses of 30 mg. twice daily (20 mg. per kilogram daily) of "marsilid," and for 21 days with doses of 15 mg. twice daily (9 mg. per kilogram daily) of "rimifon." Guinea pigs infected subcutaneously with virulent human tubercle bacilli and treated with "marsilid" 21 days later revealed very little evidence of tuberculosis grossly when killed 73 days after infection. Thirty days of treatment produced marked changes in the tuberculin skin reactions, which were positive at the beginning of therapy. Five guinea pigs infected by the intracerebral method, which is rapidly and uniformly fatal in untreated animals, were treated with "marsilid" and remained well during 60 days of treatment; since treatment was stopped, 4 have died and the fifth is showing progressive paralysis of the hindquarters. Rabbits infected intravenously with highly virulent bovine tubercle bacilli and treated with "marsilid" for 71 days remained well and failed to develop miliary pulmonary lesions demonstrable by roentgenography. Discontinuance of treatment, however, was followed by relapse of tuberculosis within 10 weeks.

American Surgeon, Atlanta, Ga.

18:341-436 (April) 1952

The Training of a Surgeon. L. J. Starry.—p. 343.
Unusual Bony Reaction to Faulty Intramedullary Pin. E. B. Carpenter and L. S. Miller.—p. 352.
Colostomy Stoma Tumors. E. L. Miloslavich.—p. 358.
Papillary Thyroid Cancer Originating in Thyroglossal Cyst. B. L. Aronoff.—p. 362.
Dermal Grafts in Repair of Massive Abdominal Hernias: Use of New Split-Split Flap Technic. J. O. Shaffer.—p. 372.
Multiple Cancers of Oral Cavity. L. T. Byars and R. Anderson.—p. 386.
*Inflammatory and Neoplastic Lesions of Small Intestine. K. C. Sawyer and A. E. Lubchenco.—p. 392.
Plastic Reconstruction of Trachea and Bronchi. D. L. Paulson.—p. 403.
Waterproof Plaster. M. C. Cobey.—p. 413.
Necrotizing Fasciitis. B. Wilson.—p. 416.

Lesions of the Small Intestine.—Sawyer and Lubchenco feel that too few lesions of the small intestine are diagnosed before operation or autopsy. They summarize their experience in treating 26 inflammatory and neoplastic lesions involving the jejunum and ileum. Lesions proximal to the ligament of Treitz and congenital anomalies were not included. The 13 patients with inflammatory lesions included 8 with regional ileitis, which is a nonspecific chronic recurrent granulomatous disease characterized by a necrotizing, ulcerating, inflammatory process. Abdominal pain, diarrhea, and secondary anemia are the cardinal features. Further confirmation of the diagnosis can be obtained from the roentgenographic recognition of the string sign. The treatment of choice is resection of the involved ileum and the right side of the colon with end-to-end ileotransverse colostomy. There were two patients with tuberculosis of the small intestine, two with diverticulitis, and one with periarteritis nodosa. The seven patients with benign neoplasms included two with carcinoid, two with endometrioma, and one each with lymphangioma, leiomyoma, and lipoma. Five of the six malignant lesions were carcinomas and one was a lymphoma. Carcinoma is the commonest malignant tumor of the small intestine. The symptoms are usually related to perforation, bleeding, or obstruction. The authors stress that any patient with unexplained diarrhea, intestinal bleeding, or abdominal pain should be subjected to careful clinical and roentgenologic study of the small intestine. Examination of the entire small intestine during routine laparotomy is worth while, and frequently reveals the pathological condition responsible for the patient's complaints.

Angiology, Baltimore

3:69-204 (April) 1952

*Intraarterial Priscoline Therapy for Peripheral Vascular Disturbances. H. I. Lippmann.—p. 69.
Cardiac Catheterization and Other Physiological Studies in 50 Cases of Congenital Heart Disease. P. R. Lurie, F. D. Gray Jr. and R. Whittemore.—p. 98.
Budd-Chiari's Syndrome: High Inferior Vena Caval Obstruction Demonstrated by Venography. B. Bronte-Stewart and R. H. Goetz.—p. 167.
Experimental Studies of Gastric Blood Flow: Preliminary Report. J. R. Vane and J. E. Thompson.—p. 179.
*Dicumarol: Dangerous and Rather Ineffective Drug. F. Martorell.—p. 185.
Surgical Treatment of Congenital Abnormalities of Heart. A. R. Albanese.—p. 189.
Thrombophlebitis Migrans; With Particular Reference to Thrombosis of Renal Veins. N. Vinther-Paulsen.—p. 194.

Priscoline® Intra-Arterially in Vascular Disturbances.—If priscoline® (2-benzyl-4,5-imidazoline) hydrochloride is injected rapidly into the regional artery of the human limb, an increase in blood flow can be observed through the main arterial channels, in the blood vessels of the skin, and throughout the deep tissues of the extremity. This effect lasts only a few hours, but after a series of injections it becomes more sustained. At a Bronx, N. Y., hospital 76 patients with peripheral vascular disease were treated by intra-arterial administration of priscoline.® In 11 patients who had gangrene of the heel, the lesions of 8 healed and 3 had to undergo amputation. This compares favorably with a control group of 11 cases in which 9 patients had to undergo amputation. Of 49 ischemic lesions in other parts of the extremities, 23 healed, and in 26 cases intra-arterial therapy was ineffective. In two of seven cases of acute arterial occlusion, embolism was the cause, and both of these patients recovered without trophic lesions; of the five who had thrombotic occlusions, two required an amputation. Four cases of iliofemoral thrombophlebitis with spastic arterial occlusion rapidly improved with one or several intra-arterial priscoline® injections. In four patients with intractable Raynaud's disease attacks disappeared during and for some time after intra-arterial priscoline® therapy, the noninjected arm serving as a control. In five cases of functional vascular disturbances, intra-arterial administration of priscoline® had a temporary and localized vasodilator effect. Priscoline® is injected rapidly into the artery in amounts just short of systemic reactions. The most effective injection schedule must be determined individually. The goal of intra-arterial priscoline® therapy in peripheral vascular disease is a sustained (not always maximal) vasodilatation in the extremity. This is maintained by regular injections over a period of days or weeks. Interruptions of the schedule or a clumsy injection technique that produces pain and vasoconstriction may prevent sustained vasodilatation. Contraindications to intra-arterial priscoline®

therapy are systemic reactions after intra-arterial injections of 10 mg. of priscoline® or less, a temporary decrease in local blood flow or edema, and skin maceration in an ischemic area after intra-arterial injection. Intra-arterial injection of this drug is a useful diagnostic test similar to a posterior tibial or lumbar sympathetic nerve block, and, carefully used, may be a valuable adjunct to treatment of peripheral vascular disorders.

Dangers of Bishydroxycoumarin.—From clinical observations and from experiments on rabbits Martorell deduced that the effective antithrombotic dose of bishydroxycoumarin (dicumarol®) and the hemorrhage-producing dose are too nearly the same. Although this drug has the advantage of being administered orally, its therapeutic efficacy is doubtful and the danger attendant on its administration reaches such proportions that it should be asked whether the risk is less for the patient from pulmonary embolism, which is not necessarily a complication of venous thrombosis, or from death by hemorrhage caused by the drug even under the most favorable conditions and with the most rigorous control of the prothrombin index.

Blood, New York

7:387-482 (April) 1952

Mechanism of Hemolysis in Paroxysmal Cold Hemoglobinuria: III. Erythrophagocytosis and Leukopenia. W. S. Jordan Jr., R. L. Prouty, R. W. Heinle and J. H. Dingle.—p. 387.

*Pathogenesis of Postirradiation Anemia. J. B. Kahn Jr. and J. Furth. —p. 404.

Changes in Cellular Composition of Lymph Caused by Ionizing Radiations. M. H. Ross, J. Furth and R. R. Bigelow.—p. 417.

Genetic Aspects of Sickle Cell Anemia and Microdrepanocytic Disease. E. Silvestroni and I. Bianco.—p. 429.

Blood Picture of Pyridoxine Deficiency in Monkey. K. J. Poppen, L. D. Greenberg and J. F. Rinehart.—p. 436.

Effect of Methylxanthines on Hypocoagulability Induced by Chloroform in Dog. J. B. Field, L. Graf and K. P. Link.—p. 445.

Pathogenesis of Postirradiation Anemia.—The hemolytic effect of large doses of irradiation is well established; the objective of this study was to determine whether irradiation within the lethal range injures erythrocytes in vivo. One group of rabbits was injected with radioiron-tagged erythrocytes shortly before exposure to 800 to 1,000 r and another group immediately after irradiation. A control group received the tagged erythrocytes but no irradiation. There was a drop in red cell mass in both irradiated groups as compared with the controls, but there was no difference between the two irradiated groups, i. e., between the behavior of irradiated and nonirradiated erythrocytes in irradiated hosts. These findings indicate that there is no direct effect of irradiation in the median lethal range on erythrocytes in vivo. It requires nearly lethal doses of x-rays to cause conspicuous anemia. In the fatally irradiated animals the drop in red cell mass and total circulating radioiron is precipitous; in those nonfatally irradiated the drop is gradual and relatively slight, even though the animals may have received the same dose. Increase of specific organ activity of the liver and spleen of irradiated animals can be correlated with hemosiderin deposits and congestion. Deposition of hemosiderin is a consequence of irradiation, its degree increasing with the effectiveness of the irradiation. In rabbits the erythrocyte masses obtained by two direct isotopic techniques (P^{32} and Fe^{59}) and by one indirect technique (T-1824 dye) differ by constant ratios. The Fe^{59}:P^{32} ratio is 0.89; the Fe^{59} values are regarded as correct. With the aid of conversion factors either technique can be used. If an indirect technique is employed and the erythrocyte mass is estimated on the basis of plasma volume measurements, it is necessary to calculate first the average body hematocrit value. This is done by multiplying the large vessel hematocrit by a conversion factor, which is 0.83 in normal rabbits. The authors conclude that irradiation at or below the median lethal dose does not hemolyze erythrocytes directly, but some change caused by massive irradiation results in increased destruction of erythrocytes. It is postulated that this change is damage to the capillary wall causing diversion of erythrocytes into tissue spaces and lymphatics, resulting in injury of some erythrocytes. Thus, the anemia of irradiation is in part relative, in part absolute.

Gastroenterology, Baltimore

20:375-534 (March) 1952

Protection of Liver by Dietary Factors. C. H. Best, W. S. Hartroft and E. A. Sellers.—p. 375.

Use of Lipotropic Factors in Treatment of Liver Disease. D. Cayer and W. E. Cornatzer.—p. 385.

*Effects of Diet and Choline on Fatty Infiltration of Human Liver. J. Post, J. G. Benton, R. Breakstone and J. Hoffman.—p. 403.

Plasma Antithrombin Titer in Incipient and Advanced Liver Failure. I. Innerfield, A. Angrist and L. J. Boyd.—p. 417.

Studies on Non-Parietal Component of Gastric Secretion in Humans: Part I. Variations in Electrolytes and Dissolved Mucin of Gastric Juice Following Insulin Stimulation. G. B. J. Glass, L. J. Boyd, I. J. Drekter and A. Heisler.—p. 430.

Id.: Part II. Present Concept of "Alkaline Constituent" of Gastric Juice. G. B. J. Glass and L. J. Boyd.—p. 442.

Studies on Pepsin Secretion: II. Effect of Vagal Resection for Duodenal Ulcer. D. T. Book, A. B. Chinn and A. J. Beams.—p. 458.

Banthine for Peptic Ulcer: Clinical and Physiologic Considerations. Preliminary Report. A. Winkelstein.—p. 464.

Gastric Mucosa in Acute Infectious Hepatitis. J. R. Loughead and F. C. Golding.—p. 471.

Treatment of Gastroduodenal Ulcerative Disease and Ulcerative Colitis with Detergent Complexes. O. E. Lobstein, B. J. Hull and S. J. Fogelson.—p. 474.

Effects of Diet and Choline on Fatty Infiltration of Liver.—This report is based on studies of 17 alcoholic patients with fatty infiltration of the liver. They were hospitalized, and clinical observation, liver function tests, and needle biopsies of the liver were made. They were placed on dietary schedules, and at intervals of 3 to 15 weeks the liver biopsies were repeated. The histological specimens were graded 0 to 4 plus for fat, periportal lymphocytic, and fibrous infiltration. Liver function tests were checked biweekly. These patients were not critically ill. Some were malnourished, others had jaundice, and all were in the state usually observed after cessation of excessive alcohol intake. One group of patients received the regular hospital diet of 250 gm. of carbohydrate, 75 gm. of protein, and 75 gm. of fat, supplemented with vitamins of the B complex group in a few cases, because of peripheral neuropathy and glossitis. A second group of patients was offered this diet, but the patients ate poorly and continued to drink heavily, through clandestine measures. A third group received the aforementioned diet to which choline was added. The basal diet had significant lipotropic effects in 13 patients. The ingestion by four patients of 4 to 17 gm. of choline bicarbonate with the basal diet did not increase the lipotropin effects observed with the diet alone. Continued ingestion of alcohol with poor dietary intake prevented the disappearance of fat from the liver. Thus the studies demonstrated that with intake of approximately 1 gm. of protein per kilogram of body weight effective lipotropism occurs within four weeks. Addition of two to six times as much choline as had been used previously had no added demonstrable effect, either on the clinical appearance of the patient, the liver function tests, or the cell structure of the liver.

Geriatrics, Minneapolis

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Practical Diagnosis in Preventive Geriatrics. B. V. White.—p. 87.

Therapeutic Nerve Block in Pain Syndromes of the Aged. D. L. Burdick. —p. 93.

*ACTH, Cortisone and Pregnenolone in Arthritis and Allied Diseases. T. H. McGavack.—p. 99.

Protein Requirements of Old Age. A. A. Albanese, R. A. Higgons, B. Vestal and others.—p. 109.

The Psychiatrist's Role in Care of the Aging. E. B. Allen and H. E. Clow.—p. 117.

Effects of Stress upon Cardiovascular Functions in Old Age. J. T. Flynn. —p. 123.

Transurethral Resection in Benign Hypertrophy of Prostate. C. D. Creevy.—p. 130.

Morbid Anatomy of Old Age. T. H. Howell and A. P. Piggot.—p. 137.

Corticotropin (ACTH), Cortisone, and Pregnenolone in Collagen Diseases.—Pregnenolone, cortisone, and corticotropin (ACTH) were given to 250 patients with a collagen or allied disease. Effective initial doses ranged from 400 to 1,000 mg., 75 to 150 mg., and 80 to 120 mg., and maintenance doses from 200 to 400 mg., 25 to 50 mg., and 20 to 40 mg., respectively. In patients with rheumatoid arthritis complete remission was obtained

in 10 of 40, 4 of 12, and 4 of 5 patients treated with pregnenolone, cortisone, and corticotropin, respectively. The effect of cortisone and corticotropin on the joint disturbances was much greater than that of pregnenolone, which affected only the periarticular and psychic manifestations of the disease. In patients with gout both corticotropin and cortisone were superior to pregnenolone, bringing about a quicker and more complete action. In patients with acute and chronic lupus erythematosus pregnenolone seems useless; cortisone, though valuable, may fail; and corticotropin will bring amelioration and remission. Cortisone and corticotropin were equally useful in psoriasis, scleroderma, uveitis, and asthma, whereas pregnenolone had some effect in scleroderma and psoriasis. Of 31 patients with osteoarthritis, 16 obtained considerable improvement with pregnenolone in the periarticular structures. There was a decrease in muscular spasm, and an increase in mobility but no alteration in the joint lesion itself. None of the drugs appeared to influence the articular disturbance. From the clinical point of view, the temperature becomes normal rather rapidly and abruptly with cortisone and corticotropin, whereas with pregnenolone it is not influenced in lupus erythematosus, and in the other diseases it becomes normal more or less by lysis. Cortisone and corticotropin produce eosinopenia in patients in whom they are useful, while pregnenolone does not. With cortisone and corticotropin euphoria is pronounced, and, if the drugs are administered too long, the patient may show irascibility, despondency, and true psychotic manifestations. These untoward effects on personality are avoided with prolonged use of pregnenolone. Undesirable side-effects appeared in 3 of 211 patients treated with pregnenolone, 13 of 41 treated with cortisone, and 6 of 26 treated with corticotropin.

Illinois Medical Journal, Chicago

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Management and Outlook of Coronary Disease. R. S. Berghoff.—p. 208.

Disseminated Lupus Erythematosus with Severe Thrombocytopenia in a Negro Male. I. A. Friedman, W. H. Kleinschmidt and S. O. Schwartz. —p. 212.

Indiana State Medical Assn. Journal, Indianapolis

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Fixed Drug Eruptions from Sulfadiazine. L. E. Gaul and G. B. Underwood.—p. 197.

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Treatment of Malignant Lymphomata. P. J. Fouts.—p. 297.

Malignant Tumors in Bone. C. F. Gregory.—p. 301.

Journal of Bacteriology, Baltimore

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Effect of High Energy Cathode Rays on Catalase Activity of Micrococcus Pyogenes Var. Aureus. B. E. Proctor, M. T. Coleman and S. A. Goldblith.—p. 337.

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Synthesis of Glutamic Acid and Glutamyl Polypeptide by Bacillus Anthracis: II. Effect of Carbon Dioxide on Peptide Production on Solid Media. C. B. Thorne, C. G. Gómez and R. D. Housewright.—p. 363.

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Journal of Immunology, Baltimore

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Studies of Antibody Distribution in Serum Proteins of Several Rh Antisera. J. R. Cann, R. A. Brown, J. G. Kirkwood and others.—p. 243.

Metabolic Studies of Rickettsiae: II. Studies on Pathway of Glutamate Oxidation by Purified Suspensions of Rickettsia Mooseri. C. L. Wisseman Jr., F. E. Hahn, E. B. Jackson and others.—p. 251.

Studies on Acute Disseminated Encephalomyelitis Produced Experimentally in Rhesus Monkeys: VII. Effect of Cortisone. E. A. Kabat, A. Wolf and A. E. Bezer.—p. 265.

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Effect of Thorotrast on Removal of Bacteria in Splanchnic Area of Intact Animal. S. P. Martin, G. P. Kerby and B. C. Holland.—p. 293.

Complement Fixation Tests with Homologous and Heterologous Types of Coxsackie Virus in Man. L. M. Kraft and J. L. Melnick.—p. 297.

Intranuclear Inclusion Bodies in Cultures of Human Tissue Inoculated with Varicella Vesicle Fluid. T. H. Weller and M. B. Stoddard.—p. 311.

Studies on Mode of Action of Aromatic Diamidines on Influenza and Mumps Virus in Tissue Culture. M. D. Eaton, M. E. Perry, C. G. Levenson and I. M. Gocke.—p. 321.

Journal of Investigative Dermatology, Baltimore

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Bacterial Flora of Skin: Factors Influencing Growth of Resident and Transient Organisms. D. M. Pillsbury and G. Rebell.—p. 173.

Blister Formation and Separation of Epidermis from Corium in Laboratory Animals. P. Flesch, S. B. Goldstone and F. D. Weidman.—p. 187.

Tissue Culture Studies on Human Skin: II. Comparative Effects of Certain Specific Contact Allergens on Sensitized and Non-Sensitized Human Skin. E. T. Everett, C. S. Livingood, C. M. Pomerat and F. Hu.—p. 193.

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*Pathogenesis of Tinea Capitis Due to Microsporum Audouini and Microsporum Canis: I. Gross Observations Following Inoculation of Humans. A. M. Kligman.—p. 231.

Antibiotics and Fungous Infections. M. J. Lipnik, A. M. Kligman and R. Strauss.—p. 247.

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Local Depilatory Action of Unsaturated Compounds: Effect of Human Sebum on Hair Growth. P. Flesch and S. B. Goldstone.—p. 267.

Histochemical Demonstration of Secretory Activity in Human Eccrine Sweat Glands. W. B. Shelley and H. Mescon.—p. 289.

Pathogenesis of Tinea Capitis.—The data reported in this paper were derived from work carried out at a state institution for congenital mental defectives where tinea capitis was endemic. A large number of persons living under confined circumstances could be inoculated, and the course of the disease minutely studied from its onset. In inoculations of the human scalp with Microsporum audouini and M. canis it was found that some form of minor trauma was a prerequisite for infection. About 60% of children were found to be susceptible to experimental tinea capitis due to M. audouini and M. canis. Although a somewhat smaller percentage of adults could be infected with M. audouini, the disease was trivial in this group. Tinea capitis has four phases: (1) an incubation period, (2) a period of enlargement and spread, (3) a refractory period, and (4) a period of involution. Tinea capitis consists of two distinct types of infection: (1) scalp infection, and (2) hair infection. Either may exist alone, and usually both are present in the early phase of tinea capitis. There are probably many persons with an innate resistance to the disease. In a susceptible person infection does not follow simple contact with the spores, which must be implanted into the stratum corneum. Minor trauma is hence a precondition for infection. The lower incidence of infection among girls is probably due to the fact that their long hair helps prevent the spores reaching the scalp surface. Transmission in the barber shop is possible, considering the minor trauma probably incident to combing and clipping. Boys who rub the backs of their heads against infected theater seats also are sub-

jected to ideal circumstances for acquiring the infection. It might be assumed that the exclusion of infected children from barber shops and theaters would contribute substantially to control of this disease.

Journal Lab. and Clinical Medicine, St. Louis

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Metabolism of Iron: I. Intravenous Iron Tolerance Tests in Normal Subjects and Patients with Hemochromatosis. S. E. Gitlow and M. R. Beyers.—p. 337.
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Electrolyte Changes Produced by ACTH, Cortisone and DOCA in Cirrhosis of Liver. W. H. Blahd, W. S. Adams, A. Leslie and others. —p. 393.
Estimation of Insulin Sensitivity by Modified Glucose Insulin Tolerance Test. S. S. Lazarus and B. W. Volk.—p. 404.
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Cold Hemagglutinins: Effect of Storage at —20° C A. E. Feller.—p. 440.
Hemolysis of Red Blood Cells Treated by Bacterial Filtrates in Presence of Serum and Complement. L. A. Rantz, A. Zuckerman and E. Randall.—p. 443.
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Journal of Thoracic Surgery, St. Louis

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*Simple Excision in Treatment of Pulmonary Tuberculosis. B. J. Ryan, E. M. Medlar and E. S. Welles.—p. 327.
Study to Determine Effect of Prevention of Overdistention of Remaining Lung Tissue on Elevated Right Ventricular Pressures, Following Resection of Lung Tissue in Dogs. B. C. Charbon and W. E. Adams. —p. 341.
Techniques of Endocardial Anastomosis for Circumventing Pulmonic Valve. T. J. Donovan, C. A. Hufnagel and H. H. G. Eastcott.—p. 348.
Fibrosarcoma of Diaphragm: Report of Case. P. D. Crimm and F. L. Kiechle.—p. 360.
Repair of Experimental Tracheal Defects with Fresh and Preserved Homologous Tracheal Grafts. O. G. Davies, J. M. Edmiston and H. J. McCorkle.—p. 367.
Hodgkin's Disease of Lung with Cavitation: Report of Three Cases. L. Efskind and P. Wexels.—p. 377.
Bronchial Adenoma: Case Report. H. H. Bradshaw, L. DeS. Shaffner and W. R. Deaton Jr.—p. 388.
Chondromatous Hamartoma of Lung. M. Rubin and J. Berkman.—p. 393.
Pulmonary Resection and Undecylenic Acid in Systemic Blastomycosis. J. E. T. Hopkins and J. D. Murphy.—p. 409.
Open Closure of Bronchus and Resection of Carina and of Tracheal Wall. V. O. Björk, E. Carlens and C. Crafoord.—p. 419.

Simple Excision for Pulmonary Tuberculosis.—Wedge or subsegmental resection of diseased lung areas was done in 30 patients with pulmonary tuberculosis for removal of tuberculous foci that remained after continuous daily treatment with streptomycin and *p*-aminosalicylic acid for four months or longer. Bilateral resections were done in three of these patients. Of the 30 patients, 4 had minimal pulmonary tuberculosis and none of these had shown tubercle bacilli in repeated cultures of sputum or gastric washings during hospitalization. They were operated on because minimal pulmonary tuberculosis always contains one or more necrotic lesions generally localized in the superior or posterior portions of lobes of lung, and it should be possible to remove these lesions completely by a small local excision. Of the remaining 26 patients, 16 had moderately and 10 had far-advanced pulmonary tuberculosis. None had had positive cultures of sputum or gastric contents for many weeks or months prior to surgical intervention. The amount of lung tissue to be excised, usually with disregard for the segmental anatomy of the lungs, was determined after a complete palpation of the lung had been done considering preservation of a maximum amount of functional lung. The wedge to be resected was outlined, the pleura incised a short distance beyond the disease area, and the area excised en bloc. Sutures were applied to bleeding points and bronchial leaks. Each resected specimen showed necrotic pneumonic lesions, and the cavity-bearing areas removed showed filled-in cavities with patent bronchial communications. Otherwise there were areas of scarred tissue, with extremely little evidence of unhealed non-necrotic pneumonic lesions. Postoperative cultures of sputum or fasting gastric contents were negative for tubercle bacilli. There was little change in the cardiorespiratory reserves postoperatively, as compared to preoperative findings. No postoperative tuberculous complications arose. No complications of any sort occurred in the four patients with minimal disease. As a rule, the postoperative course was benign. One year after the intervention all patients are in excellent physical condition. It is recognized that a lapse of five years may be necessary for final evaluation. The authors do not claim that their approach to the surgical problem of the tuberculous lung will eradicate all of the pulmonary disease, but it is anticipated that the small lesions left behind will cause no further trouble. The immediate results have been encouraging enough to warrant continuation of the program.

Journal of Urology, Baltimore

67:405-564 (April) 1952. **Partial Index**

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Operative Procedures for Stenosis Following Ureterosigmoidostomy. D. St. C. L. Henderson.—p. 479.
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Mucinous Carcinoma of Urachus Invading Bladder. M. S. Wessell, A. B. Kuritz, R. A. Burger and G. W. Reagan.—p. 523.
Postoperative Treatment Following Prostatic Surgery. J. B. Glanton, L. M. Orr and J. C. Hayward.—p. 533.
Clinical Effect of Estrogen Therapy on Metastatic Lesions from Carcinoma of Testis. C. H. deT. Shivers and H. D. Axilrod.—p. 537.
Solusponge as Hemostatic Agent in Urology. J. S. Ritter and H. Bloomberg.—p. 543.
Interesting Bone Changes in Plain Urograms. W. L. Fitzgerald and M. D. Thomas Jr.—p. 547.
Lipid Constituents of Human Male Reproductive Cells as Determined by Sudan Black B. R. L. Brown.—p. 557.

Bilateral Total Adrenalectomy.—Of 9 selected patients with advanced malignant hypertension and 5 with chronic nephritis, 13 were subjected to bilateral total adrenalectomy by the posterior approach, and one patient with nephritis had one adrenal removed as a first stage procedure. The patients operated on had failed to respond to medical treatment and at the same time their disease was considered too far advanced to be benefited by sympathectomy. A salt-free diet, diminution of edema by diuresis, digitalization, and sedation were fundamental preoperative measures. Additional measures for correction of renal insufficiency and electrolyte imbalance were necessary in four patients, external dialysis being used for one. Cortisone in doses of 100 mg. was given intramuscularly the night before operation and repeated the next morning before surgical intervention. During operation 100 to 200 cc. of aqueous adrenal cortical extract and 20 to 50 mg. of phenylephrine (neo-synephrine®) hydro-

chloride by intravenous drip was given as required for circulatory stability. Cortisone, 50 mg. every six hours, was given intramuscularly during the first 48 postoperative hours and then was gradually reduced to 25 to 37 mg. per day as a maintenance dose. In the late postoperative care salt depletion must be avoided by adding 3 gm. or more of sodium chloride to the diet and/or 1 mg. of desoxycorticosterone acetate per day three to six times a week as necessary to avoid weakness and hypotension. Two patients died of renal failure and two of cardiac complications of their vascular disease. Nine patients are living after complete adrenalectomy and seven of them are definitely improved both subjectively and objectively. One patient previously incapacitated for three years has been working for six months as a hospital orderly and another has resumed his work as an insurance agent. In their preliminary report the authors attribute the improvement to elimination of natural desoxycorticosterone-like factors and their administration thereafter in such a manner as to avoid excessive retention of sodium and water on the one hand and relative hypotension on the other. It has been shown that absence of the adrenal glands today may be compatible with an active existence, owing to available substitution therapy.

Kentucky State Medical Assn. Journal, Bowling Green

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Malignant Lymphomas (Lymphoblastomas): Medical Aspects—Pitfalls in Diagnosis. M. H. Boldt.—p. 150.
Less Common Surgical Lesions of Gastro-Intestinal Tract: Case Reports. L. E. Hurt.—p. 152.

Maine Medical Association Journal, Portland

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*Pulmonary Embolism by Amniotic Fluid with Severe Hemorrhagic Manifestations. F. M. Dooley and G. C. Leary.—p. 104.
X-Ray Diagnosis of Placenta Praevia. G. E. C. Logan and L. W. Conneen.—p. 108.
Perforation of Gastric Remnant 19 Months After Gastrectomy. S. F. Fox.—p. 111.
Chronic Alcoholism—Medical Problem. C. R. Glassmire.—p. 113.
Lymphosarcoma of Urinary Bladder. D. F. Marshall and F. M. Dooley. —p. 114.
*Cysts and Degenerative Changes in Menisci of Knee Joint. L. J. McDermott.—p. 116.

Pulmonary Embolism by Amniotic Fluid.—A total of only about 30 pathologically verified cases of pulmonary embolism and obstetric shock caused by amniotic fluid have been reported. The case described here was that of a woman in whom there had been some bleeding coincident with membrane rupture. Less than two hours later, she complained of difficulty in breathing, and then had generalized convulsions, and became cyanotic, hyperpneic and pulseless. Simultaneously there appeared red blood from the mouth, numerous rapidly spreading ecchymoses on the abdomen, chest, back, arms, and legs, and massive submucous and subcutaneous extravasation of blood involving the vaginal walls, perineum, and inner right thigh. All needle punctures oozed constantly. The placenta was delivered intact following normal separation. Despite administration of whole blood and supportive measures, massive pulmonary edema and coma occurred, and the patient died. This case of pulmonary amniotic fluid embolism has some factors in common with other cases, but differs in respect to the postmortem uterine lesions and the local genital symptoms. No evidence of abruptio placentae, placenta previa or accreta, or deep cervical or placental tear was present, but a large tear was found in the uterine endometrium. The shock was definitely anaphylactoid, and the skin was warm and dry. Unlike the patients in most cases, the patient rallied to a considerable extent from the initial shock. In the presence of afibrinogenemia, even massive transfusion (short of exsanguination and replacement) will be of no appreciable benefit unless fibrinogen is available. Since no distinction can be made in vivo between patients with intravascular fibrin clotting mechanisms and patients with amniotic fluid embolism, treatment of these conditions is essentially the same, and consists of measures to overcome shock, to control hemorrhagic manifestations, and to combat pulmonary edema. The availability of blood and fibrinogen is important.

Cysts and Degenerative Changes in Knee Menisci.—McDermott prefers the term menisci to semilunar cartilages, chiefly because it has been observed that these structures do not assume the characteristics of a cartilage until the age of 15 years. He had available for study a group of 50 menisci. Some of these had been removed because of clinically diagnosed cysts and others because of rupture. The remainder of the menisci were removed post mortem from patients with no evidence of disease of the knee joint, or from human embryos. Theories concerning the etiology, nature, and pathogenesis of the cysts as well as their relationship to rupture of the menisci are discussed. The following conclusions are formulated: 1. Cysts of the menisci result from several types of degeneration of the connective tissue. 2. The cysts have no specialized lining. 3. Synovial membrane is not endothelial in nature. 4. Cysts of the meniscus present histologically resemble ganglion cysts and myxomatous intracutaneous cysts. 5. There is no histological resemblance between meniscal cysts and the synovial membrane to suggest relationship between them. 6. Some of the so-called ruptures of the menisci may well be spontaneous in nature due to a degenerative lesion of these structures. 7. Cysts of the menisci may recur if the entire meniscus is not removed. 8. The relatively greater exposure of the internal meniscus to trauma may explain the greater frequency of rupture of this structure and the greater incidence of cysts in the external meniscus. 9. Trauma has little or no etiological importance in production of degenerative changes and meniscal cysts. 10. The etiology of the degenerative process responsible for the production of cysts of the menisci remains obscure.

Medical Annals of District of Columbia, Washington

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Dystocia Due to Fetal Abnormalities. R. H. Barter.—p. 181.
Management of Abnormal and Excessive Uterine Bleeding. R. Bieren. —p. 187.
Pathologic Anatomy of Degenerative Shoulder Lesions. J. S. Neviaser. —p. 194.
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Michigan State Medical Society Journal, Lansing

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Missouri State Medical Assn. Journal, St. Louis

49:293-372 (April) 1952

Acute Neurotic Syndromes of Combat, Nature and Management. L. L. Tureen.—p. 309.
Induced Hypotention in Surgery of Intracranial Vascular Anomalies: Report of 2 Cases. R. D. Woolsey and H. J. Freiheit.—p. 316.
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Intestinal Obstruction Due to Gallstones. R. H. Ruby and J. Nine-Curt.—p. 341.
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New England Journal of Medicine, Boston

246:391-434 (March 13) 1952

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246:435-476 (March 20) 1952

Multiple-Balloon-Kymograph Recording of Effect of Banthine, Belladonna and Placebos on Upper-Intestinal Motility. W. P. Chapman, A. B. French, P. S. Hoffman and C. M. Jones.—p. 435.
Arrow Wounds. J. A. Lundy.—p. 444.
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Effect of Volatile 1-Cyclohexyl-2-Methylaminopropane ("Benzedrex" Inhaler) on Patients with Coronary Arteriosclerosis. J. B. Burnett and S. M. Gundersen.—p. 449.
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246:477-522 (March 27) 1952

*Splenectomy in Leukemia and Leukosarcoma. J. H. Fisher, C. S. Welch and W. Dameshek.—p. 477.
Concomitant Brucellosis and Tuberculosis: Report of Case. J. T. Sharp, H. J. Wheelwright and P. O. Nice.—p. 485.
Nonvisualized Gall Bladder. F. Martin and A. G. Massimiano.—p. 488.
Influence of Carbonated Water on Gastric Emptying. G. Lolli, L. A. Greenberg and D. Lester.—p. 490.
Some Practical Aspects of Cancer Prevention. E. L. Wynder.—p. 492.
Van Riebeeck and Cape Town. H. R. Viets.—p. 503.

Splenectomy in Leukemia and Leukosarcoma.—Eleven of the 18 patients in this series had splenectomy for some type of leukemia, and 7 were found to have leukosarcoma. The decision to remove the spleen was made only after long observation. Nearly all patients had had roentgen therapy over the spleen to the limit of toleration. In leukemia, nitrogen mustard, urethane, triethylenemelamine, adrenocorticotropic hormone, or cortisone had been used. Hypersplenism, as manifested by cytopenic disturbances alone, was present in seven patients; five had severe hemolytic anemia; four had hemolytic anemia and cytopenic hypersplenism; and in two the spleen was removed because of its large size and painful symptoms. Size alone is not a sufficient indication for splenectomy. For the best results of splenectomy in hypersplenism the bone marrow should be hyperplastic. If the patient has required frequent transfusions to control a hemolytic anemia or severe cytopenia, splenectomy may be indicated, but a markedly diminished number of megakaryocytes or nucleated red blood cells in the bone marrow contraindicates splenectomy. Hemolytic anemia or the cytopenic disturbance was controlled for a reasonable period of time in 11 of the 18 patients, 5 patients were not benefited, and 2 died in hospital after operation. In one man, who had been observed for 18 months before operation, severe hemolytic anemia was the indication for splenectomy. Follow-up studies of the peripheral blood revealed that there was complete remission of the hemolytic anemia until death resulted from coronary occlusion. In a patient with pancytopenia, hemolytic anemia, and lymphosarcoma complete remission of the pancytopenia and hemolytic anemia persisted for two years. Another patient who had hemolytic anemia and lymphocytic leukemia responded temporarily to splenectomy. This patient was given a course of corticotropin prior to splenectomy. Other investigators recently reported striking improvement of the hemolytic process following corticotropin therapy in cases of acquired hemolytic anemia. Such treatment should probably be used in every case prior to splenectomy, with operative intervention reserved for patients who fail to respond to medical therapy. While it has been suggested that splenectomy should be performed early in the course of leukemia to obtain the best palliation, these authors do not believe that splenectomy is indicated unless the spleen is extremely bulky and is causing pain. They do not advocate the indiscriminate use of splenectomy, but advise that it should be confined to a small number of specially selected cases.

Northwest Medicine, Seattle

51:185-280 (March) 1952

Peritoneoscopy. R. E. Mullarky.—p. 207.
Management of Pigmented Nevi. H. C. Roys.—p. 211.
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Proc. Staff Meet., Mayo Clinic, Rochester, Minn.

27:137-168 (April 9) 1952

*Mortality and Survival in Cancer of Stomach: Statistical Summary of Experience of Mayo Clinic. J. Berkson, W. Walters, H. K. Gray and J. T. Priestley.—p. 137.
Problem of Gastric Cancer from Viewpoint of Internist. M. W. Comfort.—p. 151.
Advances in Surgical Treatment of Cancer of Stomach. W. Walters, H. K. Gray and J. T. Priestley.—p. 156.
Ileostomy Receptacle for Bed Patients. J. J. Berens and J. deJ. Pemberton.—p. 161.
Hypersensitivity to Heparin: Report of 3 Cases. E. W. Hauch, H. M. Carryer and D. R. Mathieson.—p. 163.

Mortality and Survival in Cancer of Stomach.—During the years from 1907 to 1949, 9,620 patients underwent operation for malignant neoplasm of the stomach at the Mayo Clinic, and it is estimated that there were in addition about 3,500 seen but not operated on. Of the total of 9,620 operations, 4,597 (47.8%) were resections, 1,327 (13.8%) were palliative operations, and 3,696 (38.4%) were exploratory laparotomies, with respective average hospital mortality rates of 13.3, 12.3, and 3.8%. The survival rates following operation are analyzed with relation to metastases, to grade of malignancy, to gastric acidity, and to sex. In order to ascertain whether the outlook for the patient with gastric cancer has improved, the records of the period 1907-1916 are compared with those of the period 1940-1949. The five year survival rate for the recent period is 35%, whereas for the earlier period it is 29%. The 10 year survival rate for the recent period is 27%, while for the earlier period it is 22%. There has also been improvement in the operability rate, resectability rate, and hospital mortality rate. In the early period, only 5 of 100 patients with gastric malignant lesions could be expected to be living five years later; in the later period the expected number living five years after diagnosis has increased to 14. However, this figure conveys a false idea of the efficacy of surgical therapy, because in the later group 20 of the 86 patients who died within 5 years were found inoperable when they were first examined, and in 36 more laparotomy revealed a lesion that was not resectable. Thus 56 of 86 of the deaths are accounted for by the patient's being seen too late for effective surgical intervention. The other 30 patients can perhaps be considered the true surgical loss, since in spite of surgical effort they do not survive more than five years. If the aforementioned 56 patients should be seen by the surgeon when resection was possible, then without any further improvement in the surgical

results, 18 survivors would be added to the present 14, more than doubling the number salvaged out of the original 100. Whether education or better diagnostic methods will accomplish this remains a problem for the future.

Rhode Island Medical Journal, Providence

35:121-176 (March) 1952

Acne Conglobata Treated with Aureomycin: Case Report. B. L. Schiff and A. B. Kern.—p. 137.
Treatment with Radioiodine: Report of Four Cases. F. J. Burns and F. C. Hickey.—p. 140.

Rocky Mountain Medical Journal, Denver

49:241-314 (March) 1952

Sewage Disposal Problem in Utah. K. B. Castleton.—p. 264.
Municipal Water Supplies of Utah. M. E. Murphy.—p. 268.
Curare in Thyroid Surgery: Preliminary Report. E. H. Dellinger.—p. 270.
Vascular and Pigmented Nevi. D. W. Macomber.—p. 272.

49:315-396 (April) 1952

SYMPOSIUM ON LUPUS ERYTHEMATOSUS

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The L. E. Phenomenon. T. W. Moffatt.—p. 339.
Treatment of Lupus Erythematosus. J. A. Philpott Jr.—p. 340.
Paranasal Sinuses. H. W. Merideth.—p. 343.
Clinical Evaluation of Banthine. F. B. McGlone.—p. 350.
Intramedullary Fixation of Fibula in Ankle Fractures. P. J. Preston. —p. 354.
Q Fever in Colorado. D. R. Barglow.—p. 357.

Southern Medical Journal, Birmingham, Ala.

45:287-380 (April) 1952

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Role of Banthine® in Management of Peptic Ulcer. A. C. Broders Jr. —p. 307.
Mechanism of Relief of Pain in Peptic Ulcer by Banthine.® C. W. Legerton Jr., E. C. Texter Jr. and J. M. Ruffin.—p. 310.
Significance of Prepyloric Lesion. C. M. Caravati, J. M. MacMillan and T. R. Hood.—p. 319.
Gallstone Obstruction of Intestine. R. L. Sanders and R. M. Pool. —p. 328.
Recent Advances in Surgery of Infancy. J. W. Duckett.—p. 333.
Elective Induction of Labor. E. P. Solomon and S. H. Starr.—p. 337.
Experiences with Rupture of Uterus in Pregnancy. O. T. West and C. R. Simmons.—p. 342.
*Appraisal of Injection Treatment of Internal Hemorrhoids. J. H. Dodson and M. H. Dodson.—p. 347.
Antifungal Antibiotics of Clinical Significance. W. E. Wooldridge. —p. 351.
Results of Use of Chloramphenicol and Other Antibiotics in Proctologic Practice. E. Boling and H. Finch.—p. 354.
Conservative Treatment of Degenerative Arthritis of Knee. O. O. Selke Jr.—p. 358.
Observations on Diabetic Therapy with Special Reference to Insulin Allergy. A. A. Herold Sr.—p. 360.
Reflections of a Professor Emeritus. G. P. Lingenfelter.—p. 364.
Organization and Objectives of the Civil Defense Blood Program. J. B. Alsever.—p. 366.
What the Physician Should Know About Rabies. L. E. Starr.—p. 370.

Injection Treatment of Internal Hemorrhoids.—The Dodsons evaluate the results they obtained by injection treatment in 697 cases of hemorrhoids. Of the 697 patients, 443 (63.3%) had recurrences within five years, and the authors suspect that the actual recurrence rate was even higher. Of the 201 patients classified as having first degree internal hemorrhoids (bleeding only), 76 (38%) required re-treatment, 62 being subjected to hemorrhoidectomy and 14 to reinjection. Of the 176 patients with second degree hemorrhoids (bleeding and protrusion that is spontaneously reduced), exactly half required re-treatment. Of the 289 with third degree internal hemorrhoids, 140 have had hemorrhoidectomies, 63 have had re-treatment by injection, and 35 with recurrent symptoms refused further treatment but were told that surgical intervention would be necessary for cure. All 31 of the patients with so-called fourth degree lesions have had recurrences. Thus curability by sclerotherapy varies in inverse proportion to the degree of prolapse of the hemorrhoids. Best results of injection treatment are obtained in uncomplicated first degree internal hemorrhoids. Second degree hemorrhoids are sometimes adequately treated by injections, but in third degree and fourth degree cases only temporary and usually incomplete results can be expected. At best, the recurrence rate with injections far exceeds that of careful surgical treatment. For cases in which surgical treatment is contraindicated or refused, sclerotherapy is a useful palliative measure.

U. S. Armed Forces Med. J., Washington, D. C.

3:503-656 (April) 1952. **Partial Index**

Treatment of Salmonella Infections with Chloramphenicol and Terramycin. L. E. Zimmerman.—p. 503.
Clinical Effects of Dextran as Plasma Volume Extender. J. H. Spence, A. R. Higgins and J. R. Kimmel.—p. 515.
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Use of Tetracaine Intravenously as Analgesic and Vasodilator. R. T. Smith and S. Whitehouse.—p. 525.
*Observations on Essentially Normal Young Men Treated with ACTH and Cortisone: III. Side Effects During Therapy. S. B. Appel, L. A. Fulton and K. D. Orr.—p. 531.
Use of ACTH in Dermatoses. C. Z. Berry.—p. 541.
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Thoracostomy Versus Thoracentesis: For Initial Drainage of Traumatic Hemothorax and Hemopneumothorax. R. B. Brown and S. A. Boyd. —p. 557.
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Pilonidal Cyst: Follow-Up Studies on 481 Patients. A. Kleiman.—p. 575.
Late Complications of Genitourinary Injuries. M. W. Arnold and I. T. Rieger.—p. 581.
One-Stage Pedicle Flaps to Repair Surface Defects of Lower Extremity. O. W. Wickstrom and J. R. Connelly.—p. 611.
Role of Physical Medicine in Management of Upper Extremity Amputee. R. C. Psaki and A. F. Mastellone.—p. 627.
Role of Psychiatry in Naval Retraining. J. M. Murphy and J. D. Grant. —p. 631.
Approach to Venereal Disease Control. E. F. Diamond.—p. 647.
Congenital Unilateral Superior Dislocation of Patella. S. L. Cohen and E. B. Reilly.—p. 655.

Normal Young Men Treated with ACTH and Cortisone.—Side-effects of corticotropin (ACTH) and cortisone were studied in young combat veterans with frostbite injuries that healed with medical care in all but one instance. Corticotropin (20 mg. in 1 liter of 5% dextrose in water or sodium chloride solution or in isotonic sodium chloride solution alone) was given to 13 patients daily over a six hour period for 31 consecutive days. Cortisone was given to 22 patients by mouth as follows: 400 mg. (100 mg. every 6 hours) for 1 day; 300 mg. (75 mg. every 6 hours) on the second day; 200 mg. (50 mg. every 6 hours) until the 12th day at which time 200 mg. (100 mg. at 8 a. m. and 8 p. m.) was given daily through the 31st day. There was a control group of 26 patients. Four patients (two in each hormone therapy group) were placed on moderate fluid and candy intake; otherwise, diet was unrestricted and contained excessive quantities of candy bars and soft drinks. There was no significant difference between the groups in regard to personal or familial illnesses, length of time in combat, or previous combat wounds. The side-effects noted in order of frequency were moon face, glucose intolerance, hypertension, acne, hirsutism, edema, and psychic changes. No untoward reactions were observed during intravenous administration of corticotropin, whether it was given slowly or rapidly. The effects of cortisone given orally did not differ from those obtained with intramuscular administration; no untoward gastrointestinal manifestations were noted. At least one side-effect was found in 83% of the group receiving hormone therapy; only in one case was the side-effect severe enough to force discontinuance of the treatment. Side-effects occurred in 43 patients who were given cortisone and in 17 who were given corticotropin. All the side-effects disappeared after the hormone treatment was discontinued; their common occurrence in essentially normal young men indicates pharmacologic effects, with moderate individual variation depending on dosage and duration of therapy rather than significant variation in end-organ response.

Wisconsin Medical Journal, Madison

51:237-336 (March) 1952

Diagnostic and Therapeutic Significance of Nasopharynx. W. H. Theobald.—p. 262.
Coarctation of Aorta. J. W. Gale.—p. 265.
Visual Aids as Adjunct in Starting Psychotherapeutic Process in Psychosomatic Conditions. O. S. English.—p. 269.

FOREIGN

Archivos Médicos de Cuba, Havana

3:129-252 (March) 1952. **Partial Index**

Treatment of Cardiac and Renal Diseases, Retinopathies, and Arteriosclerotic and Hypertensive Diseases with the Rice Diet. W. Kempner. —p. 131.
Radiological Diagnosis in Ulcerative Colitis. R. L. Hernández Beguerie. —p. 143.
*Preliminary Report on Intravenous Use of Corticotropin (ACTH) in Treatment of Shock. T. Armstrong and R. Pozo Jiménez.—p. 168.
Anticoagulant Treatment in Thrombophlebitis. W. G. Anylan, F. H. Campbell and W. C. Shingleton.—p. 173.

ACTH Intravenously in Treatment of Shock.—Corticotropin (ACTH) administered intravenously in three cases of apparently irreversible shock produced such rapid responses that they are made the subject of a preliminary report. The adrenocortical hormones are essential factors in the normal balance of organic functions, and enable the body to meet and overcome stress. Sudden exhaustion of the adrenocortical steroids and loss of their action on the vasomotor tone may be important in the onset of shock. Intravenous administration is apparently a safe, effective, and economical method of giving corticotropin, and has been used in various conditions. Corticotropin and cortisone have heretofore been used for shock following burns and in two cases of the Waterhouse-Friedrichsen syndrome. Intravenous use of corticotropin for serious shock is a new method, and the rapidity of the response obtained indicates that corticotropin has an immediate and selective action on vasomotor tone. The patients treated, all of whom were undergoing serious surgical procedures, had received the usual remedies for shock without showing any favorable response; all three were moribund. Administration of 40 mg. of corticotropin in 500 cc. of isotonic sodium chloride solution at a rapid rate (120 drops a minute) was quickly followed by return of the pulse, which had been imperceptible, restoration of arterial pressure, and resumption of normal breathing. All three patients recovered and were discharged from the hospital. No permanent neurological sequelae were noted; but in one case an excessive dose of corticotropin, made necessary by recurring signs of shock, led to temporary hypercorticism that was rapidly dissipated when administration of the drug was discontinued.

British Heart Journal, London

14:153-308 (April) 1952

Circulatory Changes in Severe Pulmonary Emphysema. J. P. D. Mounsey, L. W. Ritzmann, N. J. Selverstone and others.—p. 153.
Electrocardiogram in Normal Children and in Children with Right Ventricular Hypertrophy. J. F. Goodwin.—p. 173.
Electrocardiogram in Mitral Stenosis. J. R. Trounce.—p. 185.
Electrocardiogram in Tetralogy of Fallot. A. Woods.—p. 193.
Familial Heart Disease. L. G. Davies.—p. 206.
The Heart in Chronic Malnutrition. J. Higginson, A. D. Gillanders and J. F. Murray.—p. 213.
Pulmonary and Systemic Circulations in Congenital Heart Disease. D. C. Deuchar and R. Knebel.—p. 225.
*Acute Cardiac Infarction Without Pain. C. Papp.—p. 250.
Graphic Configuration of Apical Diastolic Murmurs. B. G. Wells. —p. 261.
Electronic Phonocardiograph Employing Double-Beam Cathode-Ray Oscillograph as Recording Device. F. W. Campbell, A. W. Sloan and A. M. Andrew.—p. 271.

Acute Cardiac Infarction Without Pain.—Acute cardiac infarction without pain is rare. In 150 cases in which coronary thrombosis with electrocardiographic signs of acute cardiac ischemia was diagnosed, Papp found seven patients in whom pain was completely absent, and in an eighth patient slight pain was present for a short time only. Three of the eight patients had congestive heart failure with cardiac infarction. Two died and at necropsy were found to have extensive arteriosclerotic heart disease with occlusion of more than one main coronary artery. The third, who survived, had a slight cardiac infarction during an attack of cardiac asthma. Acute paroxysmal dyspnea was the main symptom in all; this may overshadow coronary pain. Five patients had complete heart block during the attack. Four of them had no pain; in the fifth, who had intermittent heart block, pain appeared when normal rhythm was restored. Complete heart block was recorded in four, and lasted from one and a half hours to one week or more. The electrocardiogram indicated posterior infarction in three, anteroseptal infarction with right bundle branch block and later left bundle branch block in one, and anteroposterior infarction in one. All patients recovered; one had a small anterolateral infarction accompanied by pain, but not by heart block, 18 years later, from which he also recovered. Faintness with a pulse rate of 30 to 40 was the main clinical symptom, but complete loss of consciousness occurred only in one patient. These attacks differ from classical Stokes-Adams attacks in that ventricular standstill, ventricular tachycardia, and therefore complete loss of consciousness may be absent. Sudden fall of pulse rate accompanied by fall of blood pressure, as it occurs in complete heart block during acute cardiac infarction, may induce incomplete cerebral anoxemia; this causes faintness without loss of consciousness, but with loss of sense of pain. Prognosis is serious in cardiac infarction without pain and complicating heart failure; with complete heart block it may be less serious than is generally accepted, since transient block may be a sign of only temporary ischemia of the conducting system.

British Journal of Ophthalmology, London

36:169-224 (April) 1952. **Partial Index**

Orthoptics in Treatment of Squint. A. A. Douglas.—p. 169.
Treatment of Chemical Burns of Eye with Corvasymton. J. W. Wagenaar. —p. 202.
Glaucomatocyclitic Crises (Posner-Schlossman Syndrome). F. H. Theodore.—p. 207.
Vaccinia of Conjunctival Sac. A. B. Moffatt.—p. 211.
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British Medical Journal, London

1:725-778 (April 5) 1952

Some Recent Advances in Endocrinology. S. L. Simpson.—p. 725.
Daraprim in Treatment of Malaria: Study of Its Effects in Falciparum and Quartan Infections in West Africa. I. A. McGregor and D. A. Smith.—p. 730.
Daraprim (B.W. 50-63)—New Antimalarial: Trials in Human Volunteers. L. G. Goodwin.—p. 732.
Hypnosis in Childbirth. A. M. Michael.—p. 734.
Diabetes Mellitus in Surgical Patients. C. F. Rolland.—p. 737.
Incidence and Type Distribution of Capsulated H. Influenzae Strains. B. Dawson and K. Zinnemann.—p. 740.
Infantile Cortical Hyperostosis. W. J. Matheson and M. Markham. —p. 742.
Outbreak of Bornholm Disease in West Fife Practice. W. W. W. McNeish and C. Stewart.—p. 744.

1:779-830 (April 12) 1952

Mechanism of Anaphylaxis and Allergy. M. Rocha e Silva.—p. 779.
Enzyme at Sympathetic Nerve Endings. J. H. Burn.—p. 784.
Anaemia of Hypopituitarism. V. K. Summers.—p. 787.
*Survey of Pulmonary Embolism in a General Hospital. D. S. Short. —p. 790.
*Deafness with Use of Dihydrostreptomycin in Tuberculous Meningitis. J. T. Naismith.—p. 796.
Growth of Biparietal Diameter of Foetal Head in Last Weeks of Pregnancy. I. Macdonald.—p. 798.
Poliomyelitis in Mother and Newborn Infant. G. A. Wright and T. K. Owen.—p. 800.

Incidence of Pulmonary Embolism.—During the past decade it has been realized that most pulmonary emboli are not massive and fatal, and that they concern internists at least as much as surgeons and obstetricians. Indeed, the present study suggests that thromboembolic disease of the lung may have become the commonest of serious acute pulmonary lesions seen in general hospital practice. Pulmonary thromboembolism was diagnosed in 120 patients in 30 months, of whom 113 were in the wards of a general hospital. The incidence of pulmonary thromboembolism in this hospital was higher than that of lobar pneumonia. Pulmonary embolism was directly responsible for 30 deaths, and pulmonary infarction was an important contributory factor in 13 more. Seventy of the 120 cases were classed as medical, and four-fifths of the patients had heart disease. There were three instances (one fatal) of pulmonary embolism appearing without warning in apparently healthy subjects. In 4 of the 30 surgical cases (8 fatal) pulmonary embolism occurred when the patient first got out of bed. Among the 20 obstetrical cases (2 fatal) pulmonary embolism was nearly three times as common in those over the age of 30 as in those under 30. Pulmonary embolism was seen only once in the absence of obvious femoral

thrombosis or some complication of pregnancy or delivery. Pleuritic pain and hemoptysis are the two most striking symptoms of pulmonary infarction. Pleuritic pain was noted in 65% of all cases, and was present in 90% of the surgical and obstetrical cases. Hemoptysis was noted in less than 40% of all cases. The physical signs in the chest of pulmonary infarction depend on three factors, namely, consolidation, pleurisy, and elevation of the diaphragm. Signs of pleural effusion were present in one-fifth of cases. The fluid was blood-stained in 8 of 17 cases in which it was inspected. Jaundice was observed in almost one-third of the cases of heart disease complicated by pulmonary infarction. A paroxysm of auricular fibrillation was precipitated by pulmonary infarction in five cases. In several patients with congestive heart failure the symptoms were slight, and the presence of pulmonary infarction was overlooked. In postoperative and puerperal patients the condition was often misdiagnosed as pleurisy, pulmonary collapse, or pneumonia.

Deafness from Dihydrostreptomycin in Tuberculous Meningitis.—The results obtained in 26 cases in which streptomycin was administered were compared with those in 51 cases in which dihydrostreptomycin was given. Two-thirds of the patients treated with dihydrostreptomycin recovered, and one-half of those treated with streptomycin. While half of the survivors treated with dihydrostreptomycin were deaf, only 1 of 13 survivors in the streptomycin series had impaired hearing.

Deutsche medizinische Wochenschrift, Stuttgart

77:477-516 (April 18) 1952. Partial Index

Surgery of the Heart. E. K. Frey.—p. 477.
So-Called Arteriomesenterial Duodenal Closure. R. Geissendörfer.—p. 483.
Functional Problems in Cardiac and Pulmonary Disorders and Remarks on Surgery of the Heart and of Lung. H. W. Knipping.—p. 487.
*Surgical and Cardiologic Problems and Surgical Treatment of Stenosed Mitral Valves. A. Lezius and E. Gadermann.—p. 491.
Exclusion Anastomosis in Inoperable Carcinoma of Esophagus and Cardia. A. Gütgemann.—p. 497.
*Splenectomy in Therapy of Subacute Bacterial Endocarditis. K. Fellinger and W. Weissel.—p. 499.

Surgical Treatment of Mitral Stenosis.—The aim of the surgical treatment of mitral stenosis is not only to overcome the stenosis but also to preserve the closure function of the mitral valves. In the mild form of endocarditis, the stenosed orifice is usually a narrow oval, the classical button-hole stenosis, whereas in the severe form of endocarditis, the orifice is not oval, but round, irregular or triangular. Surgical correction of mitral stenosis is effected by splitting the margins of the coalescent cusps in the line of the former axis, that is, in the commissures. The authors mention Bailey, Brock, Harken, and O'Neill as having described techniques of commissurotomies or valvulotomies, and say that splitting is done most effectively with the finger equipped with a special knife, the finger being the basic instrument. Splitting of the commissures not only counteracts the stenosis but also produces functioning valves capable of closure. Injury to the valves outside of the commissures must be carefully avoided, because surgically produced defects in the valves may impair their closure. After commenting on several other problems, particularly the danger of postoperative acute mitral insufficiency, which may be brought on by the reduced tolerance of the left ventricle, the authors describe observations on seven patients in whom they performed operations for mitral stenosis. The patients ranged in age from 18 to 45 years. All patients experienced objective improvement, including those who had had decompensation for a long time and who had the corresponding anatomic and clinical changes. Severe myocardial lesions, even those in the region of the overloaded, hypertrophied and dilated right ventricle, and absolute arrhythmia after embolism, are not contraindications to the operation. It is essential, however, that no florid endocarditic process exists.

Splenectomy in Subacute Bacterial Endocarditis.—Although splenectomy was used in treatment of subacute bacterial endocarditis long before effective antibacterial therapy by means of antibiotics had become possible, now it is resorted to occasionally as an additional measure and in cases in which the antibiotics prove ineffective. In the 11 cases analyzed in this paper, splenectomy was done after treatment with antibiotics had failed. Clinical cure followed splenectomy in three of these cases, and in two others cure followed later, the fever subsiding only after a course of streptomycin, which had not been tried before splenectomy. The six other patients died despite splenectomy, but in one of these cure of the endocarditis could be proved by autopsy. There was no primary surgical mortality in these cases. Thromboembolic complications were not increased by splenectomy; at any rate, in the cases described here, the increase in thrombocytes that followed splenectomy did not result in thromboembolism. Even renal insufficiency is not an absolute contraindication to splenectomy. The time at which splenectomy is done seems important for the success of this measure, operation having been done in the successful cases during or after the first attack or relapse. However, the patients in whom splenectomy had proved successful had also received more penicillin and streptomycin. The authors make some suggestions on the possible mode of action of splenectomy, but complete clarification will require further observation and investigation.

77:517-572 (April 25) 1952. Partial Index

Kidney and Hypertension. E. Randerath and A. Bohle.—p. 517.
Prognosis of Acute Diffuse Glomerulonephritis. H. Sarre and H. Mahr.—p. 522.
Humoral Reactions of Blood in Tuberculous Patients. P. Klee, H. Hörlein and K. Jahnke.—p. 525.
*Recovery from Tuberculous Meningitis with Combined Treatment with Streptomycin and *p*-Aminosalicylic Acid in 90% of 36 Cases. W. Löffler, S. Moeschlin and H. Zollikofer.—p. 542.
*Behavior of Intestine Following Treatment with Chloromycetin. F. Sandmann.—p. 557.

Recovery from Tuberculous Meningitis with Chemotherapy.—Combined treatment with streptomycin and *p*-aminosalicylic acid was employed in 23 male and 13 female patients between the ages of 6 and 54 with tuberculous meningitis. Streptomycin was given intramuscularly in doses of 0.5 gm. twice a day for two months and dihydrostreptomycin, 0.5 gm. daily, for an additional four months. In addition streptomycin was given intraspinally in doses of 100 mg. daily the first week, 50 mg. daily the second to the fourth week, and then 50 mg. three times a week for one month, two times a week for three months, and once a week for two additional months. *p*-Aminosalicylic acid was given by intravenous drip in doses of 40 gm. daily the first week, 30 gm. daily the second to the eighth week, and 12 to 14 gm. intravenously five days a week and orally two days a week for four months. Of the 36 patients who were followed for 3½ to 38½ months, 31 were free of symptoms, 2 were still under treatment, and 3 had died of meningitis. Of the three patients who died, treatment was not started until the 20th day in one, and was discontinued too early in the other two at their own request. Of the 36 patients, 9 had associated miliary tuberculosis and 7 of them recovered. Complete blocking of cerebrospinal fluid, which had been observed frequently in patients treated with streptomycin alone, did not occur in any of the patients, and partial blocking occurred in only one patient in whom combined treatment was started on the 15th day. Bilateral impairment of the vestibular nerve occurred in 12 patients, and severe impairment of the eighth cranial nerve in 3. Of the 34 patients followed for one to three years, 3 died and 31 recovered, an average recovery rate of 90%, the best recovery rate so far recorded for tuberculous meningitis in patients followed for long periods. If one considers only the 23 patients in whom the presence of tubercle bacilli in the cerebrospinal fluid was established by culture, animal experiment, or direct detection, there were only three fatal cases after a one to three years' follow-up. Among the patients who recovered from meningitis was one with bilateral tuberculosis of the kidneys who no longer had symptoms and whose working capacity was restored. Complete recovery also resulted from 14 months' treatment with a total dose of 3,724 gm. of *p*-aminosalicylic acid intravenously and 1,737 gm. orally in an apparently hopeless case with paralysis of bladder and rectum and paraplegia. At present *p*-aminosalicylic acid administered by intravenous drip and combined with streptomycin is to be considered the method of choice for the treatment of tuberculous meningitis, miliary tuberculosis, and other severe tuberculous conditions.

Intestinal Upset After Treatment with Chloramphenicol.—Of 21 nursing infants between the ages of two and six months with pertussis treated effectively with chloramphenicol (chloromycetin®), seven had intestinal upset within 14 days after the discontinuation of therapy. Reduction of the bacterial flora in the intestines caused by the drug may result in dyspeptic disturbances, with recurrent increase of the bacterial flora after discontinuation of therapy. To 37 nursing infants with pertussis treated with chloramphenicol, 1 tablet of living Lactobacillus acidophilus was given three to five times immediately after administration of chloramphenicol was discontinued, and in addition up to 7% beta lactose was added to the formula. The administration of living lactic acid bacteria and lactose is recommended for prevention of intestinal disturbances after administration of chloramphenicol.

East African Medical Journal, Nairobi

29:41-78 (Feb.) 1952

Treatment of Urinary Bilharzia. W. L. Barton.—p. 41.
Glaucoma. A. J. Boase.—p. 45.
Removal of Foreign Bodies by Oesophagotomy. H. T. Laycock.—p. 53.
Prosthesis. N. R. E. Fendall.—p. 55.
Fixation of Fracture of Mandible. D. Barker.—p. 57.
*Report on Case of Intermittent Claudication Treated with Hexamethonium Bromide. C. H. Gurd.—p. 58.

Hexamethonium Bromide in Intermittent Claudication.—The patient described had had several operations on the kidneys. Following the first, bilateral femoral thrombosis developed. On examination the feet were cold and the pulse of the posterior tibial, popliteal, and dorsalis pedis arteries could not be felt. Because of the risk and doubtful benefit of operation a chemical sympathectomy with hexamethonium bromide was done, starting with a small dose with gradual increments until the patient was taking 0.5 gm. three times a day. The feet became less waxy and took on a rosy pink color; no pulsation, however, could be felt. The blood pressure fell about 20 mm. in each arm. The fact that hexamethonium bromide causes vasodilatation in the lower extremity appears to favor it in the treatment of this disease.

Fortschr. Röntgenstrahlen & Röntgenpraxis, Stuttgart

76:431-566 (April) 1952. **Partial Index**

Pneumonoconiotic Changes in Graphite Workers. H. Müller.—p. 452.
*Roentgenologic Aspects of Primary Cancer of Pleura. W. Pfeifer and A. Weiss.—p. 460.
Roentgenologic Differential Diagnosis of Tumors of Duodenal Bulb. R. Bauer and H. Hartweg.—p. 468.
*Etiology of Prolapse of Gastric Mucosa in the Pylorus and Duodenal Bulb. H. Etter.—p. 485.
*Roentgenologic Symptoms of Digestive Tract Following Vagotomy. Z. Zsebök.—p. 489.
Allergy of Small Intestine. P. Buffard and L. Crozet.—p. 497.
Demonstration of Transverse Layers of the Heart. A. Vallebona.—p. 508.
Changes in Shape of Ventricle During Cardiac Function. K. Heckmann.—p. 513.
Pathologic Forms of Pulsation of Ventricles. K. Heckmann.—p. 518.
Changes in Choroid Plexus During and After Toxoplasma Encephalitis. J. Schoeps.—p. 528.

Roentgen Appearance of Primary Pleural Cancer.—Primary pleural cancer includes endothelioma, sarcoma, and carcinoma. Of the 12 primary pleural cancers observed in three years by Pfeifer and Weiss, 11 were histologically verified while the patient was alive and in the 12th the growth was morphologically identified at necropsy. The authors employ the following diagnostic procedures: (1) fluoroscopy of the thorax; (2) withdrawal of the pleural exudate by puncture; (3) induction of a diagnostic pneumothorax; (4) a "second" fluoroscopic examination in two planes of exposure; (5) thoracoscopy and biopsy through the thoracoscope from the costal and visceral pleura or, if thoracoscopy proves impossible, exploratory thoracotomy with biopsy from both pleuras. They were able to carry out these procedures without complications in all 11 patients. The roentgenogram is not pathognomonic for primary cancer of the pleura, but the following findings suggest pleural cancer: (1) thickening of visceral and costal pleuras with nodulated or granulated outline, (2) absence of displacement of heart or mediastinum toward the healthy side; in advanced cases the diseased side may show shrinkage; (3) rigidity of the thorax on the diseased side and absence of mediastinal shift during respiration, even after a pneumothorax has been made; (4) tumor nodules the size of a cherry or plum on the thickened pleura; and (5) erosions of the ribs at the level of the pleural thickening.

Etiology of Prolapse of Gastric Mucosa.—Etter discusses the roentgenologic aspects of prolapse of the gastric mucosa into the pylorus and the duodenal bulb and describes a case in which the prolapse was unusually large. It was necessary to perform gastric resection because of increasing pyloric stenosis. Examination of the surgical specimen disclosed lipomatosis of the submucous coat of the antrum, which had resulted in extensive shifting of the mucosa in relation to the muscular coat and thereby produced the mucosal prolapse.

Roentgenologic Signs in Digestive Tract After Vagotomy.—Of 110 patients who had been subjected to vagotomy, 44 were reexamined roentgenologically from 18 to 24 months later. Roentgenoscopy was done first when the stomach was empty, and then again after a contrast medium had been introduced. Severe morphologic and functional changes were demonstrable throughout the digestive tract. Severe hypertrophic gastritis, disturbances in tonus and motility of the small intestine, and dyskinesia of the colon were the most important disturbances observed in patients following vagotomy. The author comments on the nature and possible etiology of these signs on the basis of his own observations and those reported in the literature.

Lancet, London

1:729-774 (April 12) 1952

Pathology and Treatment of Portal Hypertension. R. M. Walker.—p. 729.
Incompatible Transfusions: Their Causes and Prevention. G. Discombe.—p. 734.
*Effect of Adrenocorticotropic Hormone on Survival of Homografts. W. J. H. Butterfield, A. M. Williams and E. I. Evans.—p. 737.
Mysoline: New Drug in Treatment of Epilepsy. R. Handley and A. S. R. Stewart.—p. 742.
*Hypoplasia and Aplasia of Vagina Treated with Oestrogenic Hormone Implants. H. Ripman.—p. 744.
Pulsus Paradoxus. A. C. Dornhorst, P. Howard and G. L. Leathart.—p. 746.
Bone-Marrow Cultures of Koch's Bacillus. C. Choremis and S. Pantazis.—p. 748.
Sternal Osteomyelitis. D. Vellacott.—p. 749.

ACTH and Survival of Homografts.—Homografts in man and animals do not survive permanently because the host forms antibodies to the foreign proteins they contain. Since it was found that the use of corticotropin (ACTH) and cortisone alters the antigen-antibody relationships, the authors studied the effect of corticotropin on the survival of homografts in one man, one woman, and one girl with third degree burns of the trunk and thighs. None had had corticotropin or adrenocortical hormone therapy previously, and all had good adrenocortical reserves. When autografts and homografts were implanted, 100 mg. and 50 mg. of corticotropin were given daily to the adult patients and the child, respectively. Autografts and homografts took well, but the former grew and survived, whereas the latter degenerated in the woman after 11 weeks, and in the child after 51 days. In the man, who died, some of the homografts had died before his death. It is believed that, had he lived, the other homografts would not have survived because sections taken from them after death showed a very thin epithelium and absence of well-formed rete pegs. The length of survival of the homografts seemed to be related to the intensity of adrenocortical response. Corticotropin did not prevent bacterial invasion and clinical signs of infection, nor did it increase the percentage take of delayed autografts. High granulations grew over the burned areas. Side-effects attributable to corticotropin were moon face, mental disorientation, glycosuria, and, in the two adults, a diabetic state. Corticotropin prolonged but did not perpetuate the survival of homografts on deep flame burns. Early skin closure is, therefore, as urgent now as it was before the discovery of this hormone.

Estrogenic Hormone Implants in Vaginal Hypoplasia and Aplasia.—Estrogenic hormones were implanted in a 21-year-old married woman with severe vaginal hypoplasia and in a 24-year-old married woman with congenital vaginal aplasia. The first patient was actually a female castrate, her right ovary

having been removed when she was three years old because of a cyst, and there was evidence of ovarian deficiency. Eight 25 mg. pellets of estradiol implanted subcutaneously in the thigh brought about improvement that became more pronounced after three 100 mg. pellets of stilbestrol were also implanted subcutaneously in the thigh 11 months later. In a follow-up three years later, sexual intercourse was described as satisfactory, and the husband, who prior to the treatment had considered seeking an annulment of the marriage, regarded their relationship as normal. The second patient, who presumably had no ovarian tissue, was almost certainly a male pseudohermaphrodite. Three 100 mg. pellets of estradiol, and six months later six 50 mg. pellets of estradiol were implanted subcutaneously in the thigh of the patient. The improvement was pronounced, and during a follow-up nine months later she reported that sexual relations were being accomplished with ease. It appears that implants of estrogenic hormones may be valuable therapy for patients with congenital vaginal aplasia, since many of them are deficient in ovarian function. Moreover, with this treatment, hospitalization, surgical intervention, and application of instruments to the genitalia are avoided.

Lyon Chirurgical

47:257-384 (April) 1952. **Partial Index**

*Hypertension Associated with or Due to Tuberculosis of Adrenal Glands. R. Leriche.—p. 257.
Treatment of So-Called Central Pain. P. Wertheimer.—p. 260.
*Compression of Common Bile Duct Due to Chronic Pancreatitis; Diagnosis and Treatment. P. Mallet-Guy, L. Eicholz and R. Almasque Dedeu.—p. 279.
Surgical Aspects of Silicotuberculosis. A. Bonniot.—p. 305.

Hypertension and Tuberculosis of Adrenals.—Left adrenalectomy combined with bilateral subdiaphragmatic sympathectomy was performed on a 37-year-old woman with essential hypertension. The blood pressure was restored to normal. The patient resumed her work and was in good health eight months after the surgical intervention. Microscopic examination of the removed adrenal gland revealed pronounced hyperplasia of the adrenal medulla associated with disseminated caseous nodular tubercles. These findings suggested that the patients' hypertension was conditioned by the medullary hyperplasia, which resulted from the tuberculous infection. While tuberculosis commonly produces hypocorticalism, it is rather exceptional for it to result in hypertension, demonstrating that there may be other manifestations of tuberculosis of the adrenal gland than Addison's disease.

Common Bile Duct Compression Due to Chronic Pancreatitis.—In the course of 1,575 surgical interventions on the biliary tract performed under radiomanometric control during a 10 year period 36 cases of common bile duct compression due to chronic pancreatitis were observed. The latter condition was manifested by inflammatory swelling and induration of the head of the pancreas. In 2 of the 36 cases roentgenograms and manometric readings revealed complete stenosis of the common bile duct; recovery followed choledochoduodenostomy. In 18 cases a relative stenosis of the common bile duct was demonstrated by abnormally high manometric readings and by the roentgenographic appearance of the common bile duct, which revealed a disturbance of evacuation and deformity of the portion of the common bile duct close to the pancreatic tissue, with dilatation of the upper two-thirds of this portion. A syndrome consisting of pain, chills, elevation of temperature, and icterus was observed in 12 of the 18 cases, while pain alone occurred in 6 cases. Narrowing of the common bile duct was revealed roentgenographically in the remaining 16 cases, but the manometric readings were normal; symptoms were limited to the common bile duct in 6 of these cases, and the gallbladder was involved in 10 cases. The authors emphasize that diagnosis of these various conditions may be established only by radiomanometric control during surgical intervention. Deformity of the common bile duct due to chronic pancreatitis differs considerably from that due to compression by a pancreatic cancer or to stenosis due to a tumor of the ampulla of Vater. Recovery resulted from external drainage of the biliary tract in four of seven cases in which it was performed; the three other cases were therapeutic failures. Recovery resulted from internal drainage of the biliary tract in all the 21 cases in which it was carried out. Consequently systematic internal drainage of the biliary tract is recommended by the authors. Cholecystogastrostomy is feasible only in the absence of lesions due to cholecystitis. With this exception, preference should be given to choledochoduodenostomy following cholecystectomy in cases of complete or relative stenosis, while cysticoduodenostomy is to be considered the method of choice in cases with roentgenographic evidence of stenosis of the common bile duct but normal pressure readings. This intervention is simple and harmless, and excellent results were obtained in 16 cases in which it was performed.

Medical Journal of Australia, Sydney

1:349-384 (March 15) 1952

Antibody Titre in Maternal and Infant's Serum as Indication for Treatment in Haemolytic Disease of Newborn. G. A. Kelsall and G. H. Vos.—p. 349.
*Enuresis Dyad. J. Bostock and M. Shackleton.—p. 357.
"Occupational" Fevers, Queensland, 1950-1951. J. M. Kennedy, C. R. Lulham and D. Gordon.—p. 360.
Movable Eye Implant: Description of Implant Technique Using Cutler-Hamblin Prosthesis. J. L. Bignell.—p. 365.

Enuresis.—The incidence of enuresis is considerably higher among children who have had early and rigid toilet training than among those allowed to achieve control naturally (34 of 38 as compared with 2 of 35). Severity and coercion may succeed in establishing a habit of continence, but subsequent anxiety and frustration may cause regression. Restoration or creation of a favorable psychological environment free from anxiety and with opportunities for normal development may reverse the process and reestablish control. Enuresis was noted in only two of 35 children who were subjected to severe frustration but who had not had coercive toilet training. Frustration alone, therefore, does not produce enuresis; it merely initiates it.

Minerva Medica, Turin

43:267-290 (Feb. 13) 1952

Glycuronic Acid in Arthropody. M. Paltrinieri.—p. 267.
*Action of Vitamin E in Collagen Diseases. P. Grifa.—p. 270.
*Khellin in Treatment of Angina Pectoris. A. Martelli.—p. 274.
Technical Changes in Human Inoculation with Variola Virus. G. Turletti and G. C. Angela.—p. 278.

Vitamin E in Collagen Diseases.—The mode of action of vitamin E in correcting the metabolism of the connective tissue in patients with collagen diseases is not known. The hypothesis was advanced that this vitamin and its derivatives may inhibit hyaluronidase, which is considered to be responsible for the pathological picture of these diseases. The author studied the in vivo and in vitro influence of vitamin E and tocopherols on testicular hyaluronidase. A wheal was produced in the left forearm of 15 fasting patients at complete physical rest by injecting 0.1 cc. of hyaluronidase along with 0.1 cc. of a hemoglobin solution as a dye that does not affect the enzyme. After the spreading reactions were measured, 1 gm. of water-soluble vitamin E was given (500 mg. intravenously and 500 mg. intramuscularly), and a new wheal was produced in the same forearm with the same procedure. The new spreading reactions were definitely less extensive than the first. Simultaneously 0.1 cc. of an isotonic sodium chloride solution along with 0.1 cc. of hemoglobin solution were injected in the right forearm of the same patients. These spreading areas before and after administration of vitamin E were the same. In a second study 0.1 cc. of an aqueous solution of α-tocopherol and 0.1 cc. of hyaluronidase with 0.1 cc. of hemoglobin solution were injected in the left forearm of 15 other patients, while an equal dose of an aqueous solution of α-tocopherol was injected in the right forearm of the same patients along with 0.1 cc. of an isotonic sodium chloride solution and 0.1 cc. of hemoglobin solution. The spreading reactions of the left forearm were smaller than those of the right forearm. Additional in vitro studies demonstrated that this vitamin and its derivatives inhibit the mucinolytic enzyme even in very low concentrations, and increase the antihyaluronidase activity of human serum. Thus, one important function of vitamin E and its derivatives may be to serve as

regulators of hyaluronidase activity in man. When the vitamin E levels drop below a critical concentration in the body, then the enzyme may attack its substrate. The author, in agreement with Steinberg, concludes that collagen diseases are caused by a deficiency of α-tocopherol. This may result from (*a*) insufficient intake of vitamin E, (*b*) abnormal intestinal absorption of this vitamin as seen in cases of cirrhosis of the liver, and (*c*) normal intake and absorption but abnormal use of tocopherols by the connective tissue. If this hypothesis is accepted, the good results obtained by some authors with vitamin E in patients with collagen diseases are easily understood.

Visammin in Angina Pectoris.—Visammin (khellin) was given orally to 20 patients with angina pectoris in daily doses of from 60 to 100 mg. for 3 to 12 days. All the patients were benefited, and in some the anginal attacks disappeared during the therapy. Mild nausea was the only side-effect. The electrocardiograms of some patients with mild coronary disturbances who had improved returned to normal and remained normal for six days after the therapy was interrupted, revealing a prolonged pharmacological effect of the drug. In other patients with coronary disturbances in whom anginal pain was alleviated by the drug the electrocardiograms changed only slightly. In patients with left ventricular preponderance in whom anginal attacks had become less frequent and surprising improvement had occurred, the electrocardiograms remained unchanged. The drug had a vasodilating action on the coronary system but did not influence the blood pressure of the patients.

Münchener medizinische Wochenschrift, Munich

94:681-760 (April 11) 1952. **Partial Index**

Progress and Problems in Abdominal Surgery. R. Zenker.—p. 681.
Disturbances After Surgical Intervention on Stomach. V. Hoffmann —p. 691.
Diagnosis of Isolated Mediastinal Struma. G. Börger.—p. 699.
Surgical Treatment of Scar Strictures of Esophagus. P. Patronicolas. —p. 705.
*Reduction of Surgical Blood Loss by Hexamethonium and by Postural Control. T. Hoffmann.—p. 711.

Reduction of Blood Loss During Surgical Intervention.—The C_6 and C_5 derivatives of the methonium salts (hexamethonium and pentamethonium) block the autonomic ganglions. By increasing the stimulus threshold for acetylcholine, they exert the same effect on the nerve cells as curare does on the muscles. General vasodilatation of the arterioles results in lowering of the blood pressure of various degree, depending on the individual, his posture, and the functional condition of the ganglions. Lowering of the blood pressure combined with positioning of the patient on an inclined plane with the operative area at the highest point reduces the loss of blood during surgical intervention. With systolic values of 40 to 60 mm. Hg the loss of blood may be reduced to a minimum. Consequently the amount of blood required for replacement is insignificant. It is, however, imperative that the total circulating amount of blood be maintained by immediate replacement of even the smallest loss of blood, and hyperoxygenation of the blood must be assured. The angle of the plane determines to a considerable extent the level of the blood pressure, and this makes possible controlled lowering of blood pressure. It should be emphasized that only in the hands of an experienced anesthetist is this method without risk.

Nordisk Medicin, Stockholm

47:379-410 (March 21) 1952. **Partial Index**

Cardiac Irregularities and Cardiac Arrest During Anesthesia and Operation. B. S. Pedersen.—p. 379.
*Surgical Treatment of Diseases of Heart: I. Pediatric Viewpoints. E. Mannheimer.—p. 383.
*Id.: II. Coarctation of Aorta. G. Jönsson and J. Karnell.—p. 388.
*Id.: III. Mitral Defect. L. Werkö.—p. 391.
*Id.: IV. Summarizing Viewpoints. C. Crafoord.—p. 394.
Hyperactive Carotid Sinus. L. Lindén.—p. 400.

Surgical Treatment of Heart Diseases in Children.—Mannheimer reviews the clinical diagnosis and indications for operative treatment of congenital heart disease in children, and urges that all patients with congenital heart defects be admitted to special cardiological departments for examination. He considers briefly congenital heart defects that do not produce cyanosis, such as patent Botallo's duct, coarctation of aorta, anomalies of aorta and subclavian artery, and pulmonary stenosis without an overriding aorta and without septal defects. He discusses the defects that cause cyanosis, such as the tetralogy of Fallot, pulmonary atresia with overriding aorta and defect of the interventricular septum, tricuspid atresia, and Fallot's triad. Valvulotomy by Brock's method done by Crafoord in 10 cases of pulmonary stenosis with septal defect resulted in improvement in eight cases; two patients died following the intervention. Follow-up examination of 78 cyanotic children, 76 with the tetralogy of Fallot and two with tricuspid atresia, operated on in Stockholm from late 1947 to early 1950, mainly at the age of from 2 to 10, showed 10 deaths. The mortality, however, has been decreasing steadily, and the results of the anastomosis operation in suitable cases of congenital cyanosis are considered encouraging.

Surgical Treatment of Coarctation of Aorta.—Coarctation of the aorta is often discovered accidentally. Jönsson and Karnell find that the only rational treatment consists of resection of the stenosis and suture of the aorta. Of 120 patients with coarctation of the aorta examined, 94 were operated on. There were seven deaths, but one was not attributable to the intervention. All the survivors were improved subjectively. Improvement occurs more slowly in older patients. Of the objectively demonstrable improvements, normalization of the blood pressure in arms and legs is the best sign that the anastomosis is functioning satisfactorily. Not all cases are operable. If the distal end of the aortic arch is long and wide, the condition is favorable from both the operative and prognostic viewpoint; if it is long and narrow, the prognosis is less favorable; if it is short, operation is often more difficult; and if the distal end is absent, operation is impossible. The changes in the aorta that make suturing less successful increase so much between the ages of 25 and 30 that patients over 30 are not good risks. An ideal age for operation is thought to be about 10 years. The presence of another heart defect does not in principle constitute a contraindication, and it may at times increase the indication, as when there is a patent arterial duct. If the diagnosis of coarctation of aorta is established, which can be done by simple clinical methods, and the patient is of operable age, operation should not be delayed because of the absence of subjective symptoms. Careful clinical and functional analysis, however, is necessary before operation.

Surgical Treatment of Mitral Stenosis.—The indications and contraindications for mitral commissurotomy are discussed from the standpoint of heart catheterization studies. The patients who have survived operative treatment of mitral stenosis have usually shown subjective improvement. How long the improvement will continue is not yet known; Bailey's first patients, operated on more than two years ago, are still free of symptoms. Of 19 patients with mitral stenosis operated on by Crafoord, 3 died immediately following operation, all from embolism. Moderate mitral insufficiency developed in two patients. Werkö concludes that in the majority of cases isolated mitral stenosis can be treated operatively with good results. Operation is not indicated in patients with slight narrowing of the ostium reflected in relatively insignificant symptoms. In cases of marked mitral stenosis it is important to operate early. Operation should not be done when the disability depends mainly on pulmonary changes, changes after arterial embolism, or cardiac insufficiency. The immediate operative mortality is low in young patients with uncomplicated valves, but increases with the age and with increasing involvement of the heart and circulatory system.

Summary of Surgical Treatment of Diseases of Heart.—Crafoord stresses the importance of teamwork in diagnosis and treatment of cardiovascular defects and diseases. He stresses the significance of angiocardiography and heart catheterization. When correctly carried out almost no risk is associated with these examinations. In over 1,000 angiocardiographic examinations carried out in Sweden only two deaths occurred, both in cyanotic newborn infants. Angiocardiography provides such exact information preoperatively that the surgical plan can be formulated on this basis. Heart catheterization is indispensable in the evaluation of mitral stenosis, isolated pulmonary stenosis, and cardiac defects that cause cyanosis. A smaller number of atypical, prog-

nostically more unfavorable cases of patent ductus arteriosus were diagnosed by angiocardiography and heart catheterization; about half of the patients were saved by operation. Surgical treatment of heart defects under direct visualization within a bloodless field gives the best results. The author hopes that by the aid of a machine for extracorporeal circulation and oxygenization some defects may in the near future be treated surgically with better results than at present.

Policlinico (Surg. Sect.), Rome

59:1-63 (Feb.) 1952. **Partial Index**

*Blood Coagulation Time in Patients with Portal Hypertension Following Splenorenal Anastomosis. I. Bifani, P. Casolo and L. Provenzale. —p. 1.
Streptomycin in Experimental Tuberculosis in Guinea Pigs: Histopathologic Study. E. Alati.—p. 13.
Vitamin B_6 in Vomiting Produced by Anesthesia with Ether. G. Grizi. —p. 22.

Postoperative Blood Coagulation Time in Patients with Portal Hypertension.—Studies in nine patients with portal hypertension after splenorenal venous anastomosis revealed a decrease in blood coagulation time on the sixth postoperative day that was not present on the third postoperative day. This deviation was attributed to the abrupt arrest of the hypersplenic condition with thrombocytosis due to removal of the spleen, decreased heparin activity, and increased fibrinogen. It was also suggested that this condition may result from venous thrombosis at the level of the anastomosis. This, according to many authors, is not likely, since thrombosis is more likely to occur during the immediate postoperative period when reduction of the portal hypertension through the shunt decreases the velocity of the systemic circulation and a balance is established between the portal and the systemic circulation. The authors believe, however, that this balance is not established in the immediate postoperative period, because hypercoagulability did not occur until the sixth postoperative day. If manometric tests support their hypothesis, heparin treatment will be justified 24 to 36 hours after the operation, thus avoiding the harm that may be caused by administration of heparin soon after venous shunts have been devised.

Prensa Médica Argentina, Buenos Aires

39:373-420 (Feb. 29) 1952. **Partial Index**

*Perforated Peptic Ulcer. I. Z. Villafañe and M. Meeroff.—p. 373.
Chronic Remittent Epiduritis. B. B. Spota, C. A. Bardeci and J. C. Christensen.—p. 382.
Effects of Decapsulation in Kimmelstiel-Wilson Syndrome. S. Sonzini Astudillo, A. Romero, L. A. Sargiotto and F. Loza.—p. 389.
Spinal Anesthesia Supplemented by Sodium Pentothal in Gynecological Surgery. A. Dujovich.—p. 393.

Perforated Peptic Ulcer.—Ulcer perforation may occur at any age but is commonest between the ages of 41 and 50. It is seldom seen in women; the 200 patients in this series were all men. Six patients had previously been operated on for ulcer perforation; only two had been symptom free during the interval between the first operation and the recurrence. The majority of the perforations were in the pyloric region. Peptic ulcer perforation is always serious; four patients in this series, who were operated on before the discovery of antibiotics, died. Analysis of the figures in relation to ulcer activity showed that 67% of the perforations occurred while the ulcer was silent and only 33% while it was active. Pain was a constant symptom at the outset; it was sometimes slight but usually intense. Hemorrhage is a serious complication; nausea and vomiting may or may not occur; the temperature is seldom elevated greatly; tachycardia may accompany the initial shock of the perforation, subsequently disappearing for a time and reappearing if peritonitis develops. Abdominal rigidity is the characteristic sign of ulcer perforation; it occurred in every case in this series. Referred pain and various special signs also indicate the diagnosis. Diagnostic abdominal paracentesis and classification of the fluid withdrawn are valuable aids in determining etiology and topography; radiological examination, especially with a contrast medium, sometimes reveals the site of the perforation. The principal diagnostic error consists in mistaking ulcer perforation for acute appendicitis; this error occurred in 5 of the 200 cases.

Presse Médicale, Paris

60:329-348 (March 8) 1952. **Partial Index**

Electrocardiographic Studies during Resuscitation after Cardiac Arrest. L. Binet and M. V. Strumza.—p. 329.
*Potentiation of Opiate Analgesics with Neostigmine (prostigmin®). A. Abaza and M. Grégoire.—p. 331.
Evaluation of Alimentary Factor in Obesity. R. Bory and N. Pardon. —p. 333.

Potentiation of Opiate Analgesics with Neostigmine.—The pain-relieving properties of opium derivatives are greatly increased by the simultaneous administration of neostigmine (prostigmin®), making it possible to use smaller doses of opiates and reducing the danger of habituation. Neostigmine also reduces the undesirable secondary effects of opiates, especially nausea and dryness of the mouth, and corrects the intestinal and vesical paresis following the administration of morphine alone to patients undergoing surgical treatment. True synergistic action can only be obtained by using the two medications together; when they are injected separately, the pain threshold, although somewhat increased, is much lower than when they are combined. Administration of the combined medications to a large series of patients falling into two groups—one with severe pain from inoperable cancerous lesions and the other with pain following surgical interventions and various fractures—showed that 10 mg. of chlorhydrate of morphine with 0.5 mg. of neostigmine produces analgesia of greater intensity and longer duration than the same dose of morphine alone; and that 5 mg. of chlorhydrate of morphine with 0.5 mg. of neostigmine produces analgesia substantially equivalent to that produced by 10 mg. of chlorhydrate of morphine alone. The opiate and neostigmine are mixed in the same syringe and injected subcutaneously; oral administration of neostigmine simultaneously with injection of the opiate has not been tried.

60:469-488 (April 2) 1952

*Bronchial Adenomas or Epitheliomas with Altered Stroma, Identification of Bronchial Tumor with Myoepithelial Cells. J. Delarue, R. Depierre and J. Paillas.—p. 469.
Electroshock Under Phenacemide (Phenurone®). J. Bastié and A. Fernandez.—p. 471.
*Mitral Insufficiency in Malignant Rheumatic Fever. R. Lutembacher. —p. 472.

Bronchial Adenomas or "Epitheliomas."—Extensive microscopic studies carried out by the authors for the last 10 years have confirmed their view that the so-called bronchial adenomas or carcinoid or mixed bronchial tumors are epitheliomas with altered stroma similar to the tumors that commonly arise in the salivary glands. Since they may also originate from such glands as sudoriparous glands, cervical uterine glands, perianal glands, or mammary glands, the "epitheliomas with altered stroma" are not specifically bronchial. Four main types were observed: the so-called carcinoid, the cylindroma, the pluritissular and the myoepithelial cell type. It was Leroux who demonstrated that the polymorphism of these tumors results from interaction between epithelial elements and connective tissue and various metamorphoses of the stroma. The authors' microscopic sections gave evidence of the origin of the tumors from bronchial glands. The low degree of malignancy of these tumors evidently parallels the alterations of the stroma, being responsible for the slow course and the tendency to local growth, with nearly complete absence of distant metastases. The occurrence of a myoepithelial cell tumor is reported in a man, aged 63, who died four months after the appearance of the first symptoms. Necropsy revealed that the rapidly fatal course was due to the involvement of a pulmonary vein by a bud of the tumor, which nearly projected into the left auricle. This was a manifestation of the tendency to local extension. There were no lymph node and visceral metastases. Removal of the whole tumor seems to be the most rational treatment. Thoracobronchotomy is the method of choice when the parenchyma has not been severely damaged.

Mitral Insufficiency in Malignant Rheumatic Fever.—Mitral insufficiency is reported in six children between the ages of 9 and 14 and in two young adults, aged 18 and 31, with malignant rheumatic fever. In malignant rheumatic fever, observed particularly in young persons, the mitral insufficiency depends essentially on the myocarditis while the valvular lesions are only

of secondary importance. A loud systolic murmur may be observed at the apex without a preceding muffling of the heart sounds. There is pronounced cardiomegaly and asystole. The systolic murmur is accompanied by gallop rhythm and may be temporarily masked by pericarditis. Manifestations in the joints may be insignificant or completely absent. Examination of the heart at necropsy in two of the children demonstrated mitral insufficiency in its initial stage in the absence of valvular lesions; considerable dilatation of the left ventricle and the mitral ring and particularly a profound widening of the interpapillary space revealed the part played in the insufficiency by the myocarditis. In patients between the ages of 30 and 50 the valvular lesions assume considerable importance and the development of these lesions may be observed on auscultation. As long as myocarditis is absent, the diameters of the chambers of the heart are not altered and the circulatory equilibrium is maintained. When myocarditis develops, death does not result as rapidly as in the very young patients. Consequently it is more difficult to obtain microscopic proof of the disturbed myocardial functions in adults than in children with malignant rheumatic fever.

Revista Chilena de Pediatría, Santiago

23:1-42 (Jan.) 1952

*Study of the Permeability of the Meninges in Children to Penicillin Injected Intramuscularly. C. Aguilo and F. Germany.—p. 1.
Congenital Cystic Malformation of the Common Bile Duct. H. Garces, M. Neira and A. Guzman.—p. 10.
Calcified Epithelioma of Malherbe. J. Espinosa S. and J. Altamirano P. —p. 17.
Hypersplenism. J. E. Howard.—p. 20.

Permeability of Meninges to Penicillin in Children.—The permeability of the meninges to sodium penicillin injected intramuscularly was studied in 143 children, some with normal meninges and some with meningitis; 183 determinations of the penicillin concentration in the cerebrospinal fluid were made, and the results were analyzed in relation to age and dosage. Determinations made 15, 90, and 240 minutes after intramuscular injection of penicillin in children less than 1 year old with normal meninges showed appreciable concentrations in the cerebrospinal fluid when the dose was 35,000 units per kilogram of weight. A small group of infants less than 1 day old with normal meninges were given 15,000 units per kilogram; penicillin concentrations were found in the cerebrospinal fluid 90, but not 240, minutes after the injection. Comparison of the average concentrations obtained in the newborn who received only 15,000 units per kilogram with those in the group receiving 35,000 units per kilogram showed statistically significant differences, indicating the importance of using larger doses. Greater average concentrations were found in infants less than 1 day old with normal meninges than in those from 5 to 7 days old. Normal meninges are not permeable to penicillin in children more than 1 year old; the only exception noted to this rule was in four children with first and second degree burns. Meningeal inflammation results in increased permeability; penicillin was almost always found in the cerebrospinal fluid of children with acute meningitis or tuberculous meningitis.

Revista Española de Tuberculosis, Madrid

21:1-64 (Jan.) 1952

*Cervical Ribs and Thoracoplasty. J. L. Sendón.—p. 1.
Lung Abscesses. J. Viar y Flores.—p. 7.
Completely Free Clot in an Extrapleural Pneumothorax Chamber. A. Ayerbe Vallés and M. Cuesta Palomero.—p. 19.
*Treatment of Lower Lobe Cavities. J. Tapia Sanz.—p. 27.
Study of 376 Patients Admitted During One Year to a Sanatorium Without a Surgical Service: Clinical and Epidemiological Deductions. M. Valdes, F. Martin, and M. Mangas.—p. 41.

Cervical Ribs and Thoracoplasty.—The extensive use of surgical procedures in treating thoracic affections, especially pulmonary tuberculosis, gives practical importance to the study of cervical ribs. They may escape observation at operation, and since they often prevent collapse of the lung when undetected, a careful radiological study should be made of every patient who is to undergo thoracoplasty to determine whether they exist. They may be complete or incomplete and long or short. A long cervical rib requires resection, because it is in effect the first thoracic rib; resection of a short cervical rib is not always necessary. Extrafascial apicolysis, however, cannot be properly accomplished without resecting the cervical rib if there is one, regardless of its length. Technical complications may arise from the depth at which the rib is found; its relation to the brachial plexus and the subclavian artery, which varies according to the rib type and which must be known in detail if the intervention is to be carried out with confidence; and finally from the difficulty usually encountered in freeing it because its consistency is not firm and it yields at the slightest pressure from the chisel.

Treatment of Cavities of the Lower Lobe.—The results of pulmonary collapse obtained by phrenicectomy are better than those of streptomycin treatment in cavities of the apical segment of the lower lobe. Patients have been considered cured when for more than three years they have been free from symptoms and able to lead a completely normal life and cultures have been negative. Twenty-two patients in a series of 40 treated by phrenicectomy were cured and 4 were improved (average follow-up 66.8 months); these results are better than most of those reported heretofore. Streptomycin (average total dose 72 gm.), usually combined with *p*-aminosalicylic acid, was given to 30 patients with cavities in the apical segment of the lower lobe; only 10 cures were obtained, and in these the follow-up was limited to a few months. Phrenicectomy was used without regard to the duration of the cavity; only recent, nonfibrous cavities were treated with streptomycin. Marked improvement in the general condition and symptoms of the patients, with reduction in the size of the cavities, was an immediate result of streptomycin therapy, either alone or with *p*-aminosalicylic acid; later, in some cases, the cavity increased in size again. Cavities of the apical segment of the lower lobe should be treated with a combination of phrenicectomy and streptomycin when pneumothorax is impossible; even when pneumothorax is feasible, better results may be expected from the phrenicectomy-streptomycin treatment than from a pneumothorax-streptomycin combination.

Riforma Medica, Naples

66:169-196 (Feb. 16) 1952

Pathogenesis of Anemia in Diaphragmatic Hernia of Stomach: Presentation of a Case. E. Pagliardi.—p. 169.
Anesthesia with Nitrogen Protoxide in General Surgery. V. Sarnelli, G. Ruiz and A. Ventrella.—p. 172.
*Toxicity of Chloramphenicol (Chloromycetin®) in Therapy of Typhoid Fever. A. Vittone.—p. 177.

Toxicity of Chloramphenicol in Typhoid.—Total doses of chloramphenicol (chloromycetin®) of from 18 gm. to 71 gm. were given to patients with typhoid. The only side-effects were lesions of the tongue that appeared 5 to 8 days after treatment was begun and disappeared 15 to 20 days after it was discontinued. These lesions were similar to those observed in persons with vitamin deficiency. The patients complained of a burning sensation of the tongue, which was more pronounced during eating. Since the diet was adequate and none of them had vitamin deficiency before treatment, an interference of the drug with the vitamins was suggested. According to various authors, this may be caused by excretion of vitamins by the kidney, competitive action of the antibiotic against vitamins, especially vitamin B, blocking of the endogenous elaboration of vitamins, or the ability of the drug to destroy in a short time the intestinal bacterial flora that synthesizes vitamins. To study the influence of chloramphenicol on the bacterial flora the fluorescence of the tongue was examined under Wood's light, since it is believed that this fluorescence is due to production of porphyrin by local bacterial flora. The fluorescence appeared normal in all patients who did not receive chloramphenicol, whereas it was absent in 42 of 45 patients with tongue lesions. When these were cured, the fluorescence was again normal, thus suggesting a direct or indirect action of the antibiotic on nutritional processes. Since these lesions were rarely observed in patients with typhoid before the advent of this antibiotic, and since they disappear after chloramphenicol therapy is discontinued, the author attributes them to the toxic effect of the drug.

BOOK REVIEWS

Cardiac Emergencies and Heart Failure: Prevention and Treatment. By Arthur M. Master, M.D., Cardiologist, Mount Sinai Hospital, New York, Marvin Moser, M.D., 1st Lt., USAF (MC), Walter Reed Army Hospital, Washington, D. C., and Harry L. Jaffe, M.D., Adjunct Physician, Cardiology, Mount Sinai Hospital, New York. Cloth. $3. Pp. 159, with 13 illustrations. Lea & Febiger, 600 S. Washington Sq., Philadelphia 6, 1952.

The sudden development of a condition that requires prompt and intelligent treatment is a common occurrence in cardiac disorders. Ready access to information on how to treat a patient at that time is very important to the practicing physician. He wants precise directions for handling the emergency and not a learned treatise on the mechanisms involved. In this small book, Dr. Master and his group, out of their long experience in the treatment of cardiac patients at Mount Sinai Hospital in New York and in private practice, have provided for the general practitioner just what he needs to know in the management of the cardiac emergencies. In spite of the small size of this book, a broad field of therapy is covered. In the nine chapters, the following subjects are considered: arrhythmias, acute heart failure, coronary artery insufficiency, coronary artery thrombosis, syncope, hypertensive crises, surgical emergencies, and traumatic heart diseases. A few well-chosen illustrations and tables supplement the text. Although this book is simply written and concise, it is still up-to-date, including a discussion of the important new remedies, such as procaine amide hydrochloride in the treatment of arrhythmias and mercaptomerin (thiomerin®) sodium in the treatment of congestive heart failure. The practicing physician will welcome this practical little reference book on the treatment of cardiac emergencies.

The Human Blood Groups Utilized in Disputed Paternity Cases and Criminal Proceedings. By P. H. Andresen, Chief, Municipal Blood Bank, Bispebjerg Hospital, Copenhagen. Cloth. $3.75. Pp. 114. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto, 2B, 1952.

The objective of this book dealing with the human blood groups is, according to Andresen, to discuss the practical application and medicolegal significance of the subject. This material as is presented does not require too much knowledge of biology, and thus the information should be understood quite readily by physicians, lawyers, and trained technical personnel. The reader is introduced to a review of the Landsteiner system of blood grouping, the various subgroups, the M-N system, and the Rh system.

The author discusses the medicolegal utilization of blood groups in disputed paternity cases. It is pointed out that blood group determinations must be performed by specialists possessing wide training in the scientific and practical bases of blood group determinations and who are also thoroughly familiar with forensic medicine and the ordinary problems connected with the use of biologic tests for judicial purposes. Of the three essential rules governing the interpretation of disputed paternity cases, Andresen points out that although the newborn infant's blood group is not fully developed, renewed examination somewhat later is required only in exceptional cases. As a rule, a baby should be 1 month of age before the blood group is determined. This note by Andresen is exceedingly important: "In Denmark, all medico-legal laboratory tests are performed at the University Institute of Legal Medicine in Copenhagen—with the exception of the actual toxicological analyses, which are done at the University Institute of Pharmacology. This means that all tests are performed in an institution, economically as well as administratively, independent of law courts and police." We in this country can profit tremendously in this regard.

This book is highly recommended to all who are interested in the subject of human blood groups.

The reviews here published have been prepared by competent authorities and do not represent the opinions of any official bodies unless specifically stated.

Doctors in Blue: The Medical History of the Union Army in the Civil War. By George Worthington Adams. Cloth. $4. Pp. 253, with illustrations. Henry Schuman, Inc., Publishers, 20 E. 70th St., New York 21, 1952.

In the first few chapters of this book is a sad story of mismanagement at the start of the Civil War brought about by the lack of an effective system of finding the wounded on the battlefield and of a hospital system whereby they could be properly cared for. The military personnel for the north that gathered in the wounded at first were simply volunteers from various units of the army, almost wholly untrained in medical work. Many of the physicians at this time were volunteers from civil life who came and went more or less at their own convenience. Civilian teamsters, hired to drive ambulances, ran away or broke into the liquor supplies and behaved abominably, refusing to give water to the wounded, refusing to put the wounded in ambulances, and in some cases even going through the pockets of their helpless passengers. From this "frightful state of disorder" Surgeon General William A. Hammond concluded that the army had to have an ambulance corps controlled by the medical department rather than by the Quartermaster Corps. It was nearly four years, however, before this was brought about, largely through the strenuous effort of civilian reformers led by Dr. Henry I. Bowditch of Boston whose wounded son was brought off the battlefield on a horse; when at last an ambulance reached him, it was without water and its driver would procure none. When young Bowditch died of his injury, his father "went into battle" against the War Department's apathy, and he never ceased fighting until the Ambulance Corps Act of 1864 was on the statute books. Previously, however, Jonathan Letterman, a regular army medical officer, had tried to improve the situation by organizing the supply system on the divisional basis and by organizing an ambulance and field corps for the Army of the Potomac. He set up a system of divisional hospitals and provided for division of labor among the medical officers attached to each hospital. The ambulance details now were trained daily. Letterman set up tent hospitals organized by divisions but grouped together to make a corps hospital with one medical officer in command of all. The Letterman ambulance system reached its peak of development on Aug. 24, 1863, with the issuance of a general order that made the Army corps the normal ambulance unit and laid down details for management of the ambulances. Letterman's ambulance service for the Army of the Potomac became a model for other armies; in fact, it was the basis of the ambulance service of most of the armies of the world until World War I. J. Marion Sims, an American surgeon, was decorated by France for having introduced it into the French Army during the War of 1870. A typical Letterman division hospital train consisted of 14 army wagons and 4 medical wagons loaded with 22 hospital tents and medical supplies and equipment considered sufficient for the care of more than 7,000 men in a division. Thus, the mismanagement of the wounded in the early battles of the war evolved from confusion to an orderly system.

Having in mind our present advancements in surgical technique and new drugs effective against infection, the medical treatment of so many sick and wounded men during our Civil War now seems crude. Chloroform was the chief anesthetic. Throughout the four years some 80,000 general anesthetics are said to have been given with 37 deaths resulting from the chloroform, 4 from ether, and 2 from a mixture of the two anesthetics. It is interesting to learn that maggot therapy was rediscovered in the Civil War, only to be forgotten, then rediscovered in World War I, and now almost forgotten again. The one great orthopedic contribution to the Civil War was the splint, invented by Surgeon John T. Hodgen of St. Louis, a device that is still in use, providing extension and preventing contraction of the limb and giving comfort to the patient. Pyemia, tetanus, "surgical fevers," erysipelas, typhoid, dysentery, malaria, and gangrene were serious problems. Tetanus flared up alarmingly in the field hospital at the battle of Antietam, no doubt largely because the hospital was an old stable, the floor of which had

been 2 ft. deep in manure. Many of the wounded at the Battle of the Wilderness were bedded on the floors of Fredericksburg stables. Tetanus, however, was relatively rare, the number of cases being given as 505 with a mortality of 89%. With all their flaws, the Civil War hospitals, the author says, may be considered a credit to a nation, which in four years had created a vast system of 136,000 beds.

The medical record of the Civil War, on the whole, the author says, was good. This has not been generally realized, partly because the war took place before bacteriology and aseptic surgery made some of the war's medical accomplishments seem "piddling" or "irrelevant." The Civil War's morbidity and mortality rates are said to have been 2,435 and 53.4 per thousand respectively.

The author did much research before writing this book, and many of his sources of information comprise an appendix at the close of his book. It seems that he well deserved the degree for which this material was first presented as a doctoral dissertation in history at Harvard University.

Psychotherapy of Psychosis. By Gustav Bychowski, M.D., Assistant Clinical Professor of Psychiatry, New York University College of Medicine, New York. Cloth. $5.75. Pp. 328. Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1952.

The author devotes nearly all of his 34 chapters, ranging in topic from the personality of the psychiatrist to problems and prospectives, to a review of current psychoanalytic theories and techniques in the therapy of the so-called functional psychoses. He bows to other schools of thought only occasionally, e. g., in an obscure section in the phenomenology of Husserl, Minkowski, and Kronfield and in occasional passages in which Bleuler, Schneider, and Goldstein are quoted to the effect that schizophrenia may, after all, be a constitutional, metabolic, or neurophysiological disorder. Bychowski also admits *pari passu* that hypnotism "with strong suggestion," pharmaconarcosis, and even insulin therapy might be helpful as ancillary techniques of treatment, but gives no specific directions as to how to employ these in clinical practice. Instead, the author attempts to combine an outmoded Kraepelinian nosology with a welter of Freudian metapsychology expressed in the usual jargon of "id," "narcissistic identification," "weak ego core," "counter-cachexis," "primordial introjection," and similar terms vaguely meaningful to the tolerant lexicographer of psychoanalysis but for the most part mercifully beyond the ken of the general practitioners.

A few quotations from only 10 pages of the book will suffice to illustrate its style and content. Page 14: "A patient, seemingly possessed of complete indifference, could produce a strong emotional reaction either temporary or of long duration"; page 16 ff.: "The schizophrenic is affected in his vital dynamics and is thus deprived of the organization necessary to assimilate dynamics"; page 19: "The morbid emotion depersonalizes the ego and shifts the accent to the other person in whose place one would rather like to be"; page 20: "After all, no matter what theory one holds regarding the initial and the essential disturbances in schizophrenia, still nobody could deny that schizophrenics think, speak, perceive and write with their brains like anybody else"; page 23: "By way of analysis of the stream of thought I could show that the waves of energy originating in the brain of schizophrenics have special characteristics. They are incomplete and imperfect as regards their tempo as well as the degree of their delimitation. The waves, while not directed by some superior impulse, become easily independent and are unable to reach their goal. The inhibition of the stream of cerebral energy . . ."

And so on to page 245: "The impact of the sadistic superego which time and again hits the ego and punishes it with suffering and misery seems to form the main dynamic in cases of chronic depression"; page 315: "Undoubtedly many of the so-called psychopaths are latent schizophrenics where the peculiar acting out occurs as a manifestation of split-off parts of the ego."

To nearly all nonpsychiatrists (and most modern psychiatrists and psychoanalysts) such statements will sound like conceptual mystifications and semantic confusions. Conceivably, however, to some analysts still immersed in classical animistic metapsychology they may represent nuggets of insight and erudition. Bychowsky's book is recommended only to the latter.

Contemporary Correction. Editor: Paul W. Tappan, Professor of Sociology and Lecturer in Law, New York University, New York. Cloth. $5.50. Pp. 434, with 20 illustrations. McGraw-Hill Book Company, Inc., 330 W. 42d St., New York 18; Aldwych House, Aldwych, London, W.C.2, 1951.

This book presents a comprehensive symposium on the major developments and trends in the field of correction. In the foreword Sanford Bates, commissioner of the Department of Institutions and Agencies of the state of New Jersey, says, "Our penal system cannot yet be held as a success. It is the hope of Dr. Paul Tappan and the rest of us that this volume may do something toward encouraging and stimulating more widespread and persistent effort to make it so." With this purpose in mind the editor has obtained articles by qualified leaders in their respective fields and has grouped them under five main headings: part 1, Correction: Preliminary Consideration; part 2, Administrative Organization and Classification; part 3, Programs in the Correctional Institution; part 4, Types of Correctional Institutions; part 5, Extramural Treatment. To one unfamiliar with this field the book will provide an amazing experience in the revelation of the myriad problems involved in prison life. To others it will be a welcome source of information.

Physicians will be particularly interested in two chapters under part 3; in chapter 12, on medical services, correctional medical services are discussed from the viewpoint of what medical services must be rendered an inmate during his institutional residence and what the rehabilitative effects of such services will be after the inmate's release. Both the short range and long range aspects of this program are discussed in considerable detail by Dr. Justin K. Fuller, medical consultant of the Department of Corrections of the state of California and former director of the Federal Bureau of Prisons. He states, "The situations and problems that confront a correctional medical service not only are as numerous, varied, and difficult as are those found in any public or private hospital, but present some peculiar features not common to other types of medical service. . . . Acceptable modern standards of medical service include not only the diagnosis and treatment of physical illness but also psychobiology, in its broadest sense, and research. These functions must be recognized and provided for in the correctional field because of the influence that a proper medical service may have on reducing the incidence of conduct disorder, delinquency, and crime." Chapter 14, on group therapy, further elaborates on one phase of the medical program and discusses means and methods of approach. This chapter is written by Lloyd McCorkle, director of the Highfield Project in New Jersey, formerly a group psychotherapist at the Fort Knox Rehabilitation Center for military prisoners, and a prison administrator with the U. S. Army of Occupation, Japan. His discussion contains many practical suggestions together with examples of technique used.

Understanding Heredity: An Introduction to Genetics. By Richard B. Goldschmidt. Cloth. $3.75. Pp. 228, with 49 illustrations. John Wiley & Sons, Inc., 440 Fourth Ave., New York 16; Chapman & Hall, Ltd., 37-39 Essex St., Strand, London, W.C.2, 1952.

Heredity, or the science of genetics, has developed so rapidly and so precisely within the last 50 years that it has become the most central and respected of all the biologic sciences. Furthermore, it embraces topics that are of vital concern and interest to everyone. In this small book one of the world's foremost geneticists has opened the door for everyone to this most recently developed science. The author discusses in simple but exact terms such topics as the machinery of heredity, the mode of inheritance of plant and animal characters, including some human, and the origin of new variations by mutation. Helpful illustrations and charts appear. In the concluding chapter the author gives a glimpse of the more technical facts and problems of genetics. He introduces the reader to the topics of how mutations are studied, how genes act physiologically, and how genetics contributes to an understanding of evolution. The book is not a textbook and not a reference book for the specialist. It is what its title indicates, an introduction to the exciting principles and problems of genetics for the person with little or no previous knowledge of this most fascinating and important biologic subject. The book is authoritatively and well written.

Liver Injury: Transactions of the Tenth Conference, May 21-22, 1951, New York, N. Y. Edited by F. W. Hoffbauer, M.D. Cloth. $3.75. Pp. 320, with 42 illustrations. Josiah Macy, Jr. Foundation, 565 Park Ave., New York, 1951.

This book is a verbatim report of a two day conference attended by some 25 of the leading investigators in the field of liver disease. As in all Macy Foundation conferences the discussion is centered around five or six informal papers. In this volume the following subjects are presented: serum proteins and lipids by Roy H. Turner; mechanism of action of lipotropic factors in animals by Camillo Artom and action of lipotropic factors in man by David Cayer; experimental ischemia of the liver and hepatic coma by A. M. Rappaport; microanatomy of the hepatic vascular system by B. G. Maegraith and the effect of insulin on the liver in normal and diabetic men by Sheila Sherlock, A. G. Bearn, and B. Billing; and liver disease in Jamaican children by Kenneth R. Hill. Much of the material presented represents work in progress and is unpublished. The discussion is highly informal and because of the character of the participants highly informative. This volume is particularly well illustrated with tables, graphs, and plates. It has been well edited so that it reads easily. Pertinent references are included.

This is an extremely interesting and stimulating volume, which should be read by all those interested in the field of liver disease. Although much of the material is hypothetical and is only of theoretical interest at present, it should prove of interest to anyone with an inquiring mind.

Die Bluteiweisskörper des Menschen: Untersuchungsmethoden und deren klinisch-praktische Bedeutung. Von Prof. Dr. med. Ferdinand Wuhrmann, medizinischer Chefarzt, Kantonsspital Winterthur, Zürich, und Dr. Ing. Chem. Charlie Wunderly, wissenschaftlicher Oberassistent der medizinischen Universitätsklinik Zürich. Second edition. Cloth. 43.70 Swiss francs. Pp. 387, with 145 illustrations. Benno Schwabe & Co., Klosterberg 27, Basel 10, 1952.

The second edition of this excellent compilation gives, as does the first edition, detailed data on the chemistry of the plasma proteins, qualitative and quantitative protein reactions, physical, chemical, and clinical methods of study as well as the clinical significance of the plasma proteins in different disease conditions, and the production of blood proteins. Newer material, which is extensive, includes the methods and data obtained from paper chromatography, electrophoresis, spectrophotometry, ultracentrifugation, and the measurement of combination and dissociation phenomena. The material is presented in textbook fashion, and the techniques of different methods and tests are given in detail. The statements are well documented, and the extremely free use of bibliographic references, especially the European ones, is valuable for anyone wishing to make additional studies of the material. Of value to the clinician is the section (76 pages) on blood plasma data in different disease conditions and the chapter on fibrin, globulin, and albumin variations in myeloma, leukemia, anemia, kidney, liver, gastrointestinal and skin diseases, as well as in shock and other conditions. The book should be very helpful and time saving for anyone having problems or inquiries about blood proteins.

Rheumatic Diseases Based on the Proceedings of the Seventh International Congress on Rheumatic Diseases. Prepared by Committee on Publications of American Rheumatism Association, Charles H. Slocumb, M.D., Chairman. Cloth. $12. Pp. 449, with 126 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, 1952.

This volume is prepared from the talks or abstracts of the talks that were presented at the Congress on Rheumatic Diseases held in May and June, 1949. The subject matter includes such topics as histology and biochemistry of connective tissue, hormone therapy, physical rehabilitation, orthopedic surgery, psychogenic rheumatism, experimentally induced lesions, and serologic studies. The papers have been grouped into chapters according to topic discussed.

The current thinking and practice of leaders from all over the world in clinical and laboratory research are presented. Although this material was originally presented in 1949, much of it is still pertinent and of current interest. This volume will be of value to those interested in rheumatology and will serve as a milepost along the difficult road of progress in the better understanding of rheumatic disorders.

When Doctors are Patients. Edited by Max Pinner, M.D., and Benjamin F. Miller, M.D. Cloth. $3.95. Pp. 364. W. W. Norton & Company, Inc., 101 Fifth Ave., New York 3, 1952.

This book was written by physicians who are or were patients suffering from serious chronic illnesses. Some of them write under their real names and others under pseudonyms. Some of their subjective descriptions of the diseases that attacked them are short, others are quite detailed. All of them are particularly interesting because the writers are both physicians and patients. Many of the accounts are beautifully written. They reflect a stoic attitude toward life, which persons in good health too infrequently attain. These seriously ill physicians are still carrying on the practice of medicine either from a desire to keep busy or from a sense of responsibility to their families. Some of the diseases from which they suffer are multiple sclerosis, epilepsy, hypertension, migraine, manic depressive psychosis, rheumatoid arthritis, pulmonary tuberculosis, cancer, morphine and alcohol addiction, coronary occlusion, sinusitis, an acute anxiety state, and chronic brucellosis. The reader will not only learn much from these unusually instructive case histories, but he will be inspired and made thankful that he is able to live without the burden of disabling chronic disease.

Clark's Applied Pharmacology. Revised by Andrew Wilson, M.D., Ph.D., F.R.F.P.S., and H. O. Schild, M.D., Ph.D., D.Sc., Eighth edition. Cloth. $7. Pp. 691, with 120 illustrations. Blakiston Company (division of Doubleday & Company, Inc.), 1012 Walnut St., Philadelphia 5, 1952.

In undertaking revision of this well-known text, Drs. Wilson and Schild have adhered to Professor Clark's original pattern of discussing scientific evidence for the therapeutic action of the more important drugs and emphasizing the importance of this knowledge in the clinical application of the drugs. The text has been considerably revised, so that the advances of the 12 years intervening between editions could be incorporated without appreciably lengthening the book. Each chapter concludes with a short bibliography and a selection of drugs both from official British and American publications and from "New and Non-official Remedies." Dosages throughout the text are expressed in the metric system. The book can be recommended to medical students and practitioners as a convenient-sized volume that discusses the essentials of pharmacology in a clear, understandable manner.

Advances in Enzymology and Related Subjects of Biochemistry. Volume XII. Edited by F. F. Nord. Cloth. $9.75. Pp. 570, with illustrations. Interscience Publishers, Inc., 250 Fifth Ave., New York 1; 2a Southampton Row, London, W.C.1, 1951.

This book follows the style of the previous volumes of the series. Various authorities discuss and evaluate the advances that have been made in special branches of enzymology or in some closely allied field in which the author has been active. The nine chapters in this volume include a status report on starch chemistry and the enzymes involved in starch degradation and synthesis, the hydrolysis and synthesis of acetylcholine, oxidation reduction in chloroplasts, carbon dioxide fixation by autotrophs and heterotrophes, enzyme substrate compounds, peptidase specificity, biological methylation by molds, and the reaction of borates with substances of biological interest. Each chapter contains appropriate references, and the volume contains an author and subject index. A cumulative index is also included, which lists the authors and subjects of this and the previous volumes.

Seudoartrosis. Por el Prof. M. Bastos Ansart. Cloth. Pp. 207, with 80 illustrations. Publicaciones médicas José Janés, editor, Muntaner 316, Barcelona, 1951.

This monograph, which is not a reference work, discusses the author's personal experiences with ununited fractures. There is a general discussion of etiology and pathology, followed by a consideration of clinical features. The remainder of the text is devoted to a consideration of therapy. This section covers in some detail the various operative procedures preferred by the author, and he demonstrates some good results. Other existing operative procedures of value described in texts and dissertations on the subject are mentioned only briefly or not at all. The illustrations are pertinent and of fairly good quality, and the index seems to be well detailed. There is no bibliography.

Klinische Elektrokardiographie. Von Professor Dr. Carl Korth, Direktor der medizinischen Poliklinik der Universität Erlangen. Mit einer Einführung in die Grundlagen der Elektrokardiographie und der elektrokardiographischen Technik, von Dr. Joachim Ritzmann. Fifth edition. Cloth. 25 marks. Pp. 302, with 181 illustrations. Urban & Schwarzenberg, Thierschstrasse 11, Munich 22; Meinekestr. 13, Berlin W. 15, 1952.

The fifth revised edition of this textbook of electrocardiography is a valuable addition to other recent German publications on the subject. As in previous editions a clear and concisely written text together with well-selected and well-reproduced illustrations reflects the author's great experience as a clinical electrocardiographer and teacher. Multiple chest leads and aV limb leads are widely applied, and the most important chapters are further clarified by excellent diagrams, some of which are modified or taken directly from various American texts. Only a few inconsistencies in labelling and legends need correction.

Abnormalities of contour are approached from an empirical point of view with great stress upon the type of development and of regression of changes. Vectorial analysis of the abnormal electrocardiogram, recently so much favored, is more or less omitted. Some subjects, like electrolyte imbalance, apart from changes of the calcium level, and acute cor pulmonale, would warrant more emphasis and some illustration. The chapter on cardiac irregularities is excellent, as can be expected from an author who is an "old hand" in the interpretation of complicated arrhythmias. Theoretical aspects, such as the genesis of the normal electrocardiogram, are dealt with relatively briefly, in contrast to the considerable space devoted to technical details and description of instruments. The author's view that "the string galvanometer is today only of historical interest" sounds surprising, especially since he does not hesitate to apply extensively the recent advances achieved in American centers with this type of machine.

As a whole, the book can be recommended primarily as an instructive introduction to clinical electrocardiography.

Physical Rehabilitation for Daily Living. By Edith Buchwald, M.A., A.R.P.T., Director of Rehabilitation Courses for Physical Therapists, Institute of Physical Medicine and Rehabilitation, New York University—Bellevue Medical Center. In collaboration with Howard A. Rusk, M.D., Professor and Chairman, Department of Physical Medicine and Rehabilitation, George G. Deaver, M.D., Professor of Clinical Physical Medicine and Rehabilitation, and Donald A. Covalt, M.D., Associate Professor, Physical Medicine and Rehabilitation. Cloth. $7.50. Pp. 183, with 71 illustrations. McGraw-Hill Book Company, Inc., 330 W. 42d St., New York 18; Aldwych House, Aldwych, London, W.C.2, 1952.

The purpose of this book is to present a program of basic exercise and activity for daily living that can be taught to patients with disabilities of the lower extremities. Its senior author, Edith Buchwald is a registered physical therapist and the director of rehabilitation courses for physical therapists at the Institute of Physical Medicine and Rehabilitation, New York University—Bellevue Medical Center. Her collaborators were Drs. Howard A. Rusk, George G. Deaver, and Donald A. Covalt of the same institute. The members of this team have jointly produced an illustrated manual that serves as a guide in the teaching of an "A. D. L. program" (Activities of Daily Living).

The manual contains seven chapters and is well illustrated. In chapter 1 it is pointed out that the goal of the program is functional training, which involves the physical rehabilitation of the patient in order to enable him to handle himself as sufficiently and as independently as possible. To this end, chapters are included on bed and mat exercises, wheel chair exercises, self-care, ambulation, elevation and travel on crutches, use of wheel chairs and braces, activity of daily living testing, and special equipment and furniture useful in the "A. D. L. program." This book should serve as a useful guide to any member of the rehabilitation team engaged in teaching these activities of daily living to patients.

Recreation Through Music. By Charles Leonhard, Ed.D., Associate Professor of Music, University of Illinois, Urbana. Cloth. $3. Pp. 160, with 29 illustrations. A. S. Barnes & Company, 232 Madison Ave., New York 16, 1952.

This book is of principal interest to educators and recreation directors. As its title indicates, it deals with recreation through music. The roles of making music and listening to music are discussed. The use of music by recreation leaders, the techniques for community singing and choral singing together with procedures for a sing, repertory for a song leader, instrumental classes, instrumental ensembles, and an extensive list of references and song selections are included. For the physician this book might be of special interest in relation to the use of music in occupational therapy. The book itself does not deal with this subject specifically, but a physician with occupational therapy in mind would find little difficulty in translating the materials in this volume into terms of his own needs.

Orthopaedic Appliances Atlas: A Consideration of Aids Employed in the Practice of Orthopaedic Surgery. Volume I: Braces, Splints, Shoe Alterations. Published under auspices of American Academy of Orthopaedic Surgeons, Inc., in cooperation with Office of Surgeon General, U. S. A., and Veterans Administration Department of Medicine and Surgery. Cloth. $10. Pp. 588, with 945 illustrations. J. W. Edwards, 1745 S. State St., Ann Arbor, Mich., 1952.

The purpose of this amazing atlas is to present the development of standards and technical material relative to the construction, prescription, and fitting of orthopedic appliances. It is divided into seven major parts. The first part presents a fascinating historical review. Part two, entitled "Materials and Their Use," contains a detailed discussion of the materials used in the manufacture of these appliances and presents valuable technical data concerning leather, steel and its use in orthopedics, aluminum, plastic materials, rubber, adhesives, plaster of paris, wood, industrial sewing machines in orthopedic work, tools and machines commonly used by orthopedic limb and brace makers, and engineering considerations in the design of orthopedic appliances.

Other major parts of the book consider anatomy and physiology in relation to the prescription, construction, and fitting of orthopedic appliances as well as various types of appliances that are used for the spine and trunk, upper extremity, and lower extremity. Other parts of the book are devoted to braces for the paralytic patient and to the measurements of joint motion and that of parts of the body to which a brace, splint, or prosthetic device is to be applied.

This book is probably the first such comprehensive text in the English language and is a reference book which should be in the possession of every orthopedic surgeon, physiatrist, and orthopedic appliance maker as well as any other physician concerned with the use of orthopedic appliances.

The Doctors Jacobi. By Rhoda Truax. Cloth. $3.50. Pp. 270. Little, Brown & Company, 34 Beacon St., Boston 6, 1952.

This is a warmly written, well-paced story of Dr. Abraham Jacobi, famous American pioneer pediatrician known widely in New York during the last decades of the nineteenth century as "the doctor who saves the babies," and of his wife, Dr. Mary Putnam Jacobi, who studied pharmacy in New York and medicine in Philadelphia and had the distinction of being the first woman to gain admission to the École de Médecine in Paris. The biography of these two unusual people, the husband a refugee from European politics and poverty, the wife a daughter of the publisher G. P. Putnam, comes off exceptionally well, even though some of the dialogue and detail is fictionalized. This book falls "on that neutral ground between science and popularity" and is well worth the reading time of busy medical men and women.

How to Help an Alcoholic. By Clifford J. Earle. Cloth. $1.50. Pp. 96. Westminster Press, Witherspoon Building, Philadelphia 7, 1952.

By being matter-of-fact and emphasizing the practical aspects of alcoholism and its correction this volume provides inspirational guidance. The approach is one of broad appreciation and understanding and guides alcoholics to recognize and accept their roles and thus follow courses that are most likely to end in success. How alcoholism begins, clues for its early detection, and various treatment courses that may be followed are given instructive consideration. The chapter on guidance from recovered alcoholics and the 12 steps to recovery provide "treatment" material that may well be the turning point for many alcoholics. This small volume has universal applicability.

QUERIES AND MINOR NOTES

CARDIAC MASSAGE TO OVERCOME CARDIAC ARREST

To the Editor:—*Please outline the technique for entering the chest cavity for cardiac massage to overcome cardiac arrest during a surgical procedure. What treatment is established for surgical pneumothorax that follows as a result of this procedure?* *Thomas W. Kredel, M.D., Indiana, Pa.*

Answer.—The important features in dealing with such a complication are (*a*) speed in instituting the cardiac massage and (*b*) the prevention and control of ventricular fibrillation if it should occur. To accomplish these objectives it is necessary that good exposure of the heart be rapidly obtained. Some surgeons prefer to incise the left half of the diaphragm and to enter the thorax in that way if the complication occurs during the course of an abdominal operation. Such an approach, however, does not give very satisfactory visualization of the heart and makes very difficult the application of an electric shock, if needed, to control ventricular fibrillation. It seems better, therefore, in all cases to approach the heart through an intercostal incision in the fifth or fourth left interspace. A rib spreader should then be applied in order to make the exposure of the heart adequate. Care should be exercised to avoid cutting the left internal mammary artery, which ordinarily lies within about 1 cm. lateral to the border of the sternum. After the chest wall is closed the lung should be reexpanded. This can best be accomplished by inserting two tightly fitting catheters, one anterior and one posterior, into the chest cavity to provide underwater drainage. Such a procedure will remove not only the air but also the fluid that always forms after an intrathoracic procedure. It is important to carry out the intrathoracic operation with endotracheal anesthesia. If no facilities for such anesthesia are available the use of a tightly fitting face mask may be substituted, although it is not as satisfactory as endotracheal anesthesia.

LOW BLOOD SUGAR LEVEL

To the Editor:—*A patient has a persistently low blood sugar content (67.5 mg. per 100 cc.). What could be the reason for this condition, and what can be done to correct it? Except for a feeling of weakness, he has no symptoms.*

Heinrich F. Wolf, M.D., New York.

Answer.—A blood sugar level of 67.5 mg. per 100 cc., whether fasting or at any time during the day, is a mild degree of hypoglycemia. It may have no significance, but it could be due to actual or relative hyperinsulinism, the opposite condition to diabetes. Fatigue or worry in the presence of adrenal deficiency may cause spontaneous hypoglycemia. Perhaps the patient is overworked or worries too much; if so, more rest and less worry may correct the condition. The excessive use of sweets, such as desserts, candy, or soft drinks, may cause hypoglycemia by stimulating an excessive secretion of insulin by the pancreas. The patient should reduce the cane sugar products in his diet. A high protein diet, i. e., one providing meat two or three times a day and cheese or peanut butter with crackers taken three hours after meals, is helpful in such patients who are underweight or of average weight. If the patient is overweight, he should eat not more than one slice of bread at a meal, an egg for breakfast, lean meat for luncheon and dinner, with large servings of green vegetables, and medium servings of yellow vegetables, such as carrots and turnips. Fruit juice—orange, grapefruit, or apple juice—should be given on awakening, three hours after meals, and at any time for weakness. If the symptoms persist, a six hour glucose tolerance test is indicated to determine whether the patient has actual or relative hyperinsulinism.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any official bodies unless specifically stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

SLIPPED FEMORAL EPIPHYSIS

To the Editor:—*A 15-year-old boy has a slipped femoral epiphysis that has rotated so that the head is almost entirely off the neck of the femur. His symptoms began 18 months ago. For six weeks he has been unable to walk. He has an atypical Frölich's syndrome. There is no involvement of the other hip. Do you think the position of the head could be improved by traction? Roentgenograms show the epiphyseal line to be still present, and fusion has not taken place. If the position has improved after 6 to 12 weeks of traction and the head has not fused, do you think the use of a Smith-Petersen nail would be indicated?* *M.D., Minnesota.*

Answer.—After 18 months' duration of this condition, traction on the leg would not change the position of the capital epiphysis. Skilfully applied manipulation, with the patient under anesthesia, may effect a change of position. If so, and if the restoration were considered satisfactory, a Smith-Petersen nail or suitable screw should be inserted, without splitting the head, for fixation of the head of the femur to the neck. If manipulation fails, open operation employing a cuneiform osteotomy, reposition, and nailing is indicated. Any shortening of the leg caused by an early fusion of the epiphysis thus obtained may be compensated for in part by overgrowth of the distal epiphysis. No surgeon except one highly trained in this type of work should attempt such an operation.

SIGNIFICANCE OF ARCUS SENILIS

To the Editor:—*What is the significance of a marked arcus senilis in a man 43 years old? Is there any relationship between it and atherosclerosis? Is it a sign of the aging process?*

M.D., Toronto, Canada.

Answer.—Arcus senilis is a form of lipoid deposition in the peripheral cornea; it is usually considered to be associated with senescence; however, the condition may occur early in life, and its appearance in the fourth decade is not uncommon. The relationship between arcus senilis and atherosclerosis is debatable. Boas (Arcus Senilis and Arteriosclerosis, *J. Mt. Sinai Hosp.* **12**:79 [May-June] 1945) found an appreciably higher incidence of coronary disease among those with arcus senilis than those without it. Garn and Gertler (Arcus Senilis and Serum Cholesterol Levels in the Aleut, *New England J. Med.* **242**:283 [Feb. 23] (1950) have disputed the relationship between arcus senilis and hypercholesterolemia discussed by Boas. They conclude that hypercholesterolemia or degenerative disease need not be a concomitant of arcus senilis.

EPISTAXIS AND HEART DISEASE

To the Editor:—*Since having an attack of coronary occlusion, a patient has been using neocurtasal® (a sodium free salt substitute consisting of potassium chloride, ammonium chloride, potassium formate, calcium formate, magnesium citrate, and starch), but he has had nose bleeding. Do you think the blood vessels are more fragile after neocurtasal® has been used?*

M.D., Illinois.

Answer.—Epistaxis is a common occurrence in patients with heart disease, especially when there is associated failure, hypertension, or rheumatic fever. Since it is stated that the patient had an attack of coronary occlusion, and neocurtasal® was then prescribed, presumably there was an episode of congestive failure. Neocurtasal,® which is primarily a salt of potassium chloride, is used as a substitute for salt, so that the ingestion of sodium ion may be restricted. There has been no evidence to suggest that this compound will cause increased capillary fragility that might lead to bleeding of any type. If nosebleeds are severe and occur especially from a single site, a small ulcer or erosion should be sought and if found should be treated by application of a simple chemical (silver nitrate) or electric cautery.

STIMULATION OF SPERMATOGENESIS

To the Editor:—*A man two years ago had a sperm count of 1 million per cubic centimeter, and a total semen volume of 3 cc. Results of a testicular biopsy were normal. He was given small doses of methyltestosterone, and almost complete suppression of spermatogenesis occurred. Would it be possible at present for him to have a sperm count high enough to produce a pregnancy? If pregnancy in such a case occurs, would the baby be normal?* *M.D., Ohio.*

Answer.—Testosterone may be used in the treatment of oligospermia with some hope of success if testicular biopsy shows that no irreversible changes have taken place in the germinal epithelium. Large doses are employed—50 mg. administered parenterally 3 times a week up to a total dose of 2,000 mg. or more. The initial effect is a depression in spermatogenesis leading to complete or almost complete azoospermia, but some time after therapy is discontinued a majority of the patients exhibit a "rebound" phenomenon, with sperm counts rising well above the pretreatment levels. A few of them succeed in impregnating their wives. On the other hand, in about 15% of cases the depression is not followed by a rebound, and the patients may be in a worse condition than they were before. Small doses of testosterone can depress spermatogenesis, as occurred in this case. When they are discontinued, the previous seminal values are usually restored, with no benefit accomplished and no permanent damage done.

While impregnation sometimes occurs with notably low sperm counts, in general, any reduction in numbers below the conventional figure of 60 million spermatozoa per cubic centimeter involves a corresponding reduction in relative fertility. For this reason oligospermia should be treated. In the present case it might be worth while to try the large dose testosterone method. Adjuvant measures include attention to the general health and hygiene, a high protein, high vitamin diet, and enough thyroid to keep the basal metabolic rate at or a little above the +10 level.

An alternative method for impregnation would be the preparation of a centrifuged sperm concentrate and application of this to the cervix either with a syringe or in a plastic cervical cap. The rate of miscarriage of first pregnancies among couples relieved of sterility is slightly higher than in the general population. If this hazard is escaped, the chances of having a normal baby at term will be the same as they are in other matings.

METHANTHELINE BROMIDE AND VISION

To the Editor:—*Can methantheline bromide (banthine®), 50 mg., given at bedtime, cause continued blurred vision, "circles" under the eyes, and twitching of the eyelids in a male patient 41 years of age who apparently has normal vision?* *M.D., Ohio.*

Answer.—Methantheline bromide (banthine®) causes a cholinergic blockade and will affect accommodation, if the dose is large enough, in a manner similar to atropine. When instilled into the conjunctival sac it causes pupillary dilation and cycloplegia and has an action similar to that of homatropine. It seems possible, therefore, that methantheline bromide may cause blurring of vision, severer for near objects than for distant objects, and that twitching of the eyelids may be associated with this.

FRECKLES

To the Editor:—*What are the etiology and pathogenesis of ephelides? Are there any studies on the treatment of ephelides with cortisone and corticotropin (ACTH)?*

Nehmet H. Nagle, M.D., Turkey.

Answer.—Ephelides, or freckles as they are commonly called in this country, are due to precipitation of pigment in localized patches caused by exposure to sunlight. This is often a family trait, seen mostly in blonde and redhaired persons, although it occurs also in the mulatto. Cortisone and corticotropin (ACTH) have been found to be of no value in the treatment of this condition. It is possible by the use of monobenzyl ether of hydroquinone to reduce the number of freckles temporarily.

TESTOSTERONE AND THE MALE CLIMACTERIC

To the Editor:—*In a question and answer column in a medical periodical the answer stated that giving testosterone to uncastrated elderly men seems most unwise, and that whether the "male menopause" actually exists is open to question. My reading on the subject does not coincide with this viewpoint. I would appreciate having your opinion on this subject.*

E. W. Goldstein, M.D., Pittsburgh, Pa.

This inquiry was referred to two consultants, whose respective replies follow.—Ed.

Answer.—There is a difference of opinion as to the actual existence of a condition in the elderly man comparable to the female menopause. There is not much doubt, however, that many elderly male patients develop definite psychogenic symptoms, which apparently result from changes in glandular physiology and sex hormones. Although many of these patients are definitely helped by administration of testosterone, there are others in whom androgenic therapy has no effect. Whether beneficial results from testosterone are brought about by its action as a metabolic hormone or as a sexual hormone has not been definitely determined. It should be stated, however, that long-continued treatment with testosterone in large doses might have injurious effects. Cases have been observed in which there is apparently carcinogenic action in prostatic cells.

Answer.—There is still some difference of opinion on this question; however, most of the data available indicate that giving testosterone to older men will not in itself cause carcinoma of the prostate. It may perhaps accelerate the growth of a carcinoma already present, but androgen alone will not cause normal tissue to become carcinomatous. There is enough evidence available to demonstrate that there is a male climacteric, which responds specifically to androgen therapy; however, it is not nearly as common as the menopause in the woman, and great caution must be used in arriving at the diagnosis.

STERILIZATION OF SYRINGES

To the Editor:—*Is the practice of rinsing syringes and needles in acetone or ether a satisfactory method of cold sterilization? If not, what is the preferred cold method for use by the general practitioner?*

Newton H. Reid, M.D., College Park, Md.

Answer.—The risk of causing homologous serum jaundice precludes the use of any chemical agent for disinfection of syringes and needles. There is no evidence that such agents are effective in preventing the transmission of the virus. Immersion in boiling water for 15 minutes or dry heat sterilization for an hour at 165 C (329 F) is recommended for the disinfection of previously cleaned lancets, needles, and syringes.

DISCREPANCIES IN BLOOD CELL COUNTS

To the Editor:—*I have noted discrepancies in blood cell counts performed by different laboratories. I find that one laboratory makes all red blood cell counts and hemoglobin determinations from venous blood. Another uses both venous and capillary blood, and another uses only capillary blood. Are variations in blood cell counts to be expected and, if so, to what degree?* *John T. Hecker, M.D., Cedar Rapids, Iowa.*

Answer.—From a practical standpoint, no great differences will occur between hemoglobin determinations and red blood cell counts made from venous blood and those made from capillary blood. In regard to white blood cell counts, blood from the capillaries may give somewhat higher values (1,000 to 1,500 cells per cubic millimeter) than venous blood. The discrepancies in blood cell counts performed by different laboratories are not due to differences in the location from which the blood is obtained but are the result of the great variation in accuracy and techniques existing in the different laboratories. The various factors contributing to these discrepancies are discussed in the Syllabus of Laboratory Examinations in Clinical Diagnosis (Ham, T. H., editor, Cambridge, Mass., Harvard University Press, 1950).

BRONCHIECTASIS

TO THE EDITOR:—*A 45-year-old white woman had a lobectomy for bronchiectasis two years ago. She now has bilateral involvement. Her condition remains about the same with bed rest, supportive treatment, and terramycin, 250 mg., every six hours. Without terramycin, she runs a low-grade fever. Would penicillin-sulfonamide therapy or penicillin inhalation be of any value?* *Robert L. Bestoso, M.D., Newport, R. I.*

ANSWER.—If complete bronchograms have not been obtained since operation, these should be done to determine the distribution of the remaining bronchiectasis, since certain cases, even when the disease is bilateral, are considered for surgical resection on the second side. If the distribution of the bronchiectasis in this patient is such that surgery can no longer be considered, then the objectives of treatment should be (1) to improve drainage from the bronchial tree, and (2) to eliminate infection with antibiotics. The first objective necessitates postural drainage, performed at least twice daily; undoubtedly periodic bronchoscopic aspiration would likewise be helpful in preventing stagnation of secretions. Reasonable physical activity should be allowed, unless this results in temperature elevation or undue fatigue.

Antibiotic treatment is preferably based on laboratory determination of the susceptibility of the organisms found in the sputum or, better, in secretions obtained at the time of bronchoscopy. It appears likely that systemic administration of antibiotics is more effective than administration by inhalation alone; however, for maximum effect, combined administration (systemic and inhalation) is preferred, about one-third of the total daily quantity being given by the latter method in four divided doses. Empirical use of a sulfonamide, such as gantrisin® (3,4-dimethyl-5-sulfanilamido-isoxazole) would be justified if response to antibiotics is not satisfactory. Usefulness of maintenance doses of antibiotics entails the problem of induced resistance of the organisms present, so that intensive treatment for periods of 7 to 10 days, preferably combined with bronchoscopic aspiration, followed by an interval without specific antibacterial treatment, would seem more rational.

PLASTIC INDURATION OF PENIS

TO THE EDITOR:—*About eight months ago a plastic induration on the middle of the urethral surface of the penis developed in a patient. At that time the involved area was treated with filtered roentgen rays, and the induration was greatly reduced. Later, the patient was given ten ultraviolet ray treatments, which helped somewhat. Now the induration is as large as it was before treatment. This is the first such case seen during my long practice, and I will appreciate your opinion on treatment and prognosis.*

Angelo Marcoglous, M.D., Greece.

ANSWER.—This patient has Peyronie's disease, which is sometimes called plastic induration of the penis and, also, fibrosis of Buck's fascia. The treatment of this condition is very discouraging. Diathermy and other types of local heat application over a long period of time have in some instances produced a softening of the scar tissue. Treatment with continuous doses of vitamin E in the form of eprolin® (a concentrate of natural alpha, beta, and gamma tocopherols) or tocopherol acetates, 100 to 200 mg. given 2 to 3 times a day, has in a few instances resulted in regression of the induration. This has been especially true in the patient who has Peyronie's disease and Dupuytren's contracture of the fingers simultaneously. Ultraviolet or infrared ray treatments should not be used. The best improvement to date has occurred with treatment by local irradiation with combined roentgen rays and radium topically applied by an experienced radiologist. Recently, injections of solvent material, such as hyaluronidase, have been tried, without appreciable permanent improvement. Almost every type of treatment has been used, including futile surgical attempts at incision and extirpation. The disease often disappears or improves spontaneously with no treatment. The only logical treatment, used by those who see many of these patients, is a 6 to 12 month course of vitamin E therapy and local irradiation. The lesion never becomes malignant as far as is known. This disease was thought to be rare some years ago, but in the United States, at least, it occurs in about 1% of all men over the age of 55.

TUBERCULOUS LYMPHADENITIS

TO THE EDITOR:—*A woman, aged 45, with two children, had an enlarged cervical gland under the right sternocleidomastoid muscle in 1936. It was the size of an orange. Guinea pig inoculation of material obtained surgically revealed tuberculosis. There was no recurrence until 1951, at which time the family moved from southern to northern California. The gland is now the size of a walnut. Chest roentgenograms show no tuberculosis. Roentgen therapy of the gland is being considered as the patient refuses any kind of biopsy. Is a tuberculous cervical lymph gland influenced in any way by dampness?*

Willis J. Bogue, M.D., Chico, Calif.

ANSWER.—The question of the influence of "dampness" on cervical lymph nodes is not of great importance. Dampness may cause frequent "colds," chilling, and "lowering of resistance," but the existence of a previous infection is the chief concern. The fact that the patient had a tuberculous node removed many years ago leaves little doubt about the nature of the process, since such infections may "smolder" for many years. The treatment should be that for a tuberculous node, at least until such treatment fails to be effective. In that event, a biopsy may be mandatory. X-rays can be used successfully on early tuberculous nodes, but the best treatment is the combination of streptomycin (1 gm. twice a week) and *p*-aminosalicylic acid (PAS) (12 gm. a day in four doses). If the nodes are soft and large, surgery may also be necessary.

SENSITIVITY TO RABIES VACCINE

TO THE EDITOR:—*Is there a satisfactory way to test sensitivity to rabies vaccine?*

George A. Peck, M.D., Salt Lake City.

ANSWER.—There is no reliable method for testing sensitivity to rabies vaccine. It has been presumed that severe reactions, when they occur, are due to the presence of the rabbit brain tissue in the vaccine. The frequency with which antirabies vaccination accidents occur is commonly overemphasized. Their occurrence has been variously stated to be from 1 in 9,000 to 1 in 600 persons (Los Angeles, 1940 to 1946). The problem of rabies vaccine reaction is discussed in "Correction of Summary on Rabies in 1951—Report of the Academy (of pediatrics) Committee on Immunization and Therapeutic Procedures for Acute Infectious Diseases" (*Pediatrics* **9**:336 [March] 1952).

MUMPS VACCINE

TO THE EDITOR:—*Is material for skin testing for determining immunity to mumps available? If a skin test or complement-fixation test is negative in an adult male, would you recommend using Hyland's hyperimmune mumps serum?*

Etta Link, M.D., Berkley, Mich.

ANSWER.—Material for skin testing for susceptibility to mumps is now available (Lilly). Mumps vaccine is also used for active immunization that is presumed to endure for six months to a year. The skin test is believed to be more reliable for adults than the complement fixation test. The latter is preferred in the case of children. Hyperimmune mumps serum for passive immunization is considered to be of value by some investigators. When used in large doses for treatment it is thought to reduce the frequency of orchitis.

PROTECTIVE GOGGLES

TO THE EDITOR:—*Could headache or dizziness result from the use of work goggles with clear or colored lenses, which are not fitted by prescription, by men who do not ordinarily wear glasses?* *J. M. Hesser, M.D., Benson, Ariz.*

ANSWER.—Protective lenses will not cause headache or dizziness unless a prism or cylinder is ground into the lens. If the lenses are without power they should have no action other than reducing the amount of light entering the eyes. Sometimes safety goggles, because of their weight, cause head pains if the frame has been improperly fitted.